

Treatment for Stimulant Use Disorders

UPDATED 2021

TREATMENT IMPROVEMENT PROTOCOL

TIP 33

SAMHSA

Substance Abuse and Mental Health
Services Administration

Please share your thoughts about this publication by completing a brief online survey at:

www.surveymonkey.com/r/KAPPFS

The survey takes about 7 minutes to complete and is anonymous.

Your feedback will help SAMHSA develop future products.

This page intentionally left blank.

Contents

Foreword	ix
Executive Summary	xi
Introduction	xi
Overall Key Messages	xii
Content Overview	xiii
TIP Development Participants	xvii
Consensus Panel	xvii
Field Reviewers	xviii
Resource Panel	xx
Editorial Advisory Board	xxi
Publication Information	xxiii
Chapter 1—Introduction	1
Purpose of the TIP	1
Organization of the TIP	2
Scope of the TIP	4
Current Stimulant Use in the United States	4
Importance of Science in Building Future Treatments	9
Summary	9
Chapter 2—How Stimulants Affect the Brain and Behavior	11
Substance Use Disorders	12
Neurobiology	14
The Reward System or Positive Reinforcement	14
The Stress System or Negative Reinforcement	15
Drug Craving and Memory	16
Role of Technologies	17
Stimulant Use and the Brain	19
Stimulants' Mechanisms of Action	19
General Effects of Stimulants	20
Effects of Route of Administration	22
Psychological and Neurocognitive Effects	22
Cocaine	22
Methamphetamine	25
Prescription Stimulant Medications	28
Assessment and Diagnosis	28
Summary	32



Chapter 3—Medical Aspects of Stimulant Use Disorders	33
Toxicity, Addiction, and Other Adverse Reactions	37
Intoxication	43
Clinical Manifestations and Medical Management	45
Identification and Management of Medical Complications	54
Identification and Management of Mental Complications	62
Co-Occurring Disorders and Conditions	67
Linking Treatment Programs and Medical Facilities	70
Summary	72
Chapter 4—Approaches to Treatment	73
How To Measure Effectiveness	74
Documented Psychosocial Treatment Approaches	76
Treatment Approaches With Supportive Research	83
Case Management and Coordinated Care	85
Other Interventions With Supportive Research	86
Other Models of Psychosocial Treatment	86
Clinical Issues To Consider	88
Summary	91
Chapter 5—Practical Application of Treatment Strategies	93
People With Stimulant Use Disorders Seeking Treatment	94
Treatment Needs of People With Cocaine Use Versus Methamphetamine Use Versus Prescription Stimulant Misuse	96
Maximizing Treatment Engagement	96
Assessment Procedures To Enhance Treatment Engagement	98
Staff Skills To Enhance Treatment Engagement	99
Treatment	100
Strategies for Engagement	100
Strategies for Treatment Initiation	105
Strategies for Stabilization	108
Strategies for Maintenance	113
Other Strategies Useful in Maintaining Abstinence	117
Next Steps	119
Summary	119
Chapter 6—Treatment Considerations for Special Populations	121
Racial/Ethnic Minority Populations	122
Women (Including Those Who Are Pregnant)	131
Men Who Have Sex With Men	135
Transgender and Gender Nonbinary Community	139
Adolescents	141
People Experiencing Homelessness/Unstable Housing	144

Rural Populations	145
People Involved in the Criminal Justice System	147
People Taking Medication for Opioid Use Disorder	149
People Who Inject Drugs	151
People Living With HIV/AIDS.	152
People With or At Risk for Hepatitis	155
Individuals With Co-Occurring Mental Disorders	157
Summary	163
Chapter 7—Resources	165
Resources for Counselors, Providers, and Programs	165
Publications.	168
Treatment Locators	174
Client and Family Resources.	175
Laws and Regulations.	177
Additional Resources	178
Bibliography	181

This page intentionally left blank.

Exhibits

Exhibit 1.1. Key Terms	3
Exhibit 2.1. Brain Structures Involved in the Reward System	13
Exhibit 2.2. Normal Dopamine Transmission	16
Exhibit 2.3. Continuum of Psychostimulant Activation	21
Exhibit 2.4. Acute Effects of Cocaine on Dopamine Transmission	23
Exhibit 2.5. Acute Effects of Methamphetamine on Dopamine Transmission	25
Exhibit 2.6. Key Terms	26
Exhibit 3.1. Key Terms	34
Exhibit 3.2. Effects of Route of Use for Cocaine, Methamphetamine, and Prescription Stimulants	38
Exhibit 3.3. Differences Between Cocaine, Methamphetamine, and Prescription Stimulants	39
Exhibit 3.4. Common Signs and Symptoms of Acute Stimulant Intoxication	42
Exhibit 3.5. Common Signs and Symptoms of Stimulant Withdrawal/ Abstinence Syndrome	48
Exhibit 3.6. Common Symptoms of Chronic Stimulant Use or Prescription Stimulant Misuse	52
Exhibit 3.7. Distinctive Indicators of Chronic Use of Cocaine and Methamphetamine, and Chronic Misuse of Prescription Stimulants	52
Exhibit 3.8. AGRO+ Method for Deescalation With Aggressive Patients	65
Exhibit 4.1. Stimulant Use: Managing Common Clinical Issues	89
Exhibit 5.1. Key Terms	104
Exhibit 6.1. Key Terms	139
Exhibit 6.2. Estimated Per-Act Probability of Acquiring HIV From an Infected Source by Exposure Act*	153
Exhibit 6.3. Hepatitis Risk and Prevention for People Who Use Stimulants	156

This page intentionally left blank.

Foreword

The Substance Abuse and Mental Health Services Administration (SAMHSA) is the U.S. Department of Health and Human Services agency that leads public health efforts to reduce the impact of substance abuse and mental illness on America's communities. An important component of SAMHSA's work is focused on dissemination of evidence-based practices and providing training and technical assistance to healthcare practitioners on implementation of these best practices.

The Treatment Improvement Protocol (TIP) series contributes to SAMHSA's mission by providing science-based, best-practice guidance to the behavioral health field. TIPs reflect careful consideration of all relevant clinical and health services research, demonstrated experience, and implementation requirements. Select nonfederal clinical researchers, service providers, program administrators, and patient advocates comprising each TIP's consensus panel discuss these factors, offering input on the TIP's specific topics in their areas of expertise to reach consensus on best practices. Field reviewers then assess draft content and the TIP is finalized.

The talent, dedication, and hard work that TIP panelists and reviewers bring to this highly participatory process have helped bridge the gap between the promise of research and the needs of practicing clinicians and administrators to serve, in the most scientifically sound and effective ways, people in need of care and treatment of mental and substance use disorders.

My sincere thanks to all who have contributed their time and expertise to the development of this TIP. It is my hope that clinicians will find it useful and informative to their work.

Miriam E. Delphin-Rittmon, Ph.D.

Assistant Secretary for Mental Health and Substance Use
U.S. Department of Health and Human Services
Substance Abuse and Mental Health Services Administration

This page intentionally left blank.

Executive Summary

Introduction

Since the 1980s, stimulant use has wreaked havoc on individuals and communities across the United States and has prompted strong responses from federal, state, and local governments and organizations. For example, the relatively minor problems caused by cocaine use in the 1960s and 1970s have grown to become major medical and law enforcement issues.

Similarly, the increasing use of methamphetamine (MA) has led policymakers, public officials, and service providers to increase efforts to fight its spread. For example, concerns that MA use would become epidemic led to passage of the Combat Methamphetamine Epidemic Act of 2005 and the incorporation of MA-specific provisions in the Comprehensive Addiction and Recovery Act of 2016. Misuse of prescription stimulants such as methylphenidate has also become a growing concern.

The explosive growth of stimulant use has also triggered a flurry of research. The results are tremendous advances in understanding stimulant use disorders, the basic functioning of the brain, and substance use disorders (SUDs) in general. Yet reports that describe the fundamentals of stimulant use disorder treatment and the success of various treatment interventions are still needed.

This Treatment Improvement Protocol (TIP) reviews what is currently known about treating the medical, psychiatric, and SUD-related problems associated with the use of cocaine and MA and the misuse of prescribed stimulants (such as those for the treatment of attention deficit hyperactivity disorder [ADHD]).

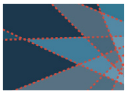
The scientifically based information in this TIP is presented in a manner that makes it accessible and relevant to behavioral health service clinicians and other frontline SUD treatment providers, including healthcare service providers (e.g., in primary care settings, in emergency departments). The TIP offers recommendations on treatment approaches, strategies for planning and initiating treatment, recommendations on how to maximize treatment engagement and retention, and strategies for initiating and maintaining abstinence. Also included are recommendations for the medical management of people who use stimulants and recommendations regarding special populations and settings.

The Substance Abuse and Mental Health Services Administration (SAMHSA) first published this TIP in 1999. SAMHSA implemented a full-scale review and revision of the original TIP. Content now addresses:

- Recent research on stimulant use disorders.
- The increasing number of overdose deaths in the United States attributable to cocaine and MA (especially when combined with other substances, like synthetic and semisynthetic opioids).
- The rise in the use and misuse of prescription stimulants (leading to increased risk and incidence of diversion).

This TIP revision:

- Uses terminology that is person centered and aligned with language in the latest edition of the *Diagnostic and Statistical Manual of Mental Disorders*.
- Incorporates findings from research published since 2010 (and where possible, since 2016).
- Includes key messages at the beginning of every chapter to guide readers in understanding from the outset the core content they are about to read.
- Updates statistics and related information about stimulant use, treatment, overdose, and legislation in the United States.



- Provides a more focused discussion of the neurobiology of stimulant use disorders than the original TIP's broad primer on the topic.
- Reflects updated empirical evidence that supports using contingency management (CM), cognitive-behavioral therapy (CBT), community reinforcement, and motivational interviewing (MI) to treat stimulant use disorders—as well as recent evidence for other nonpharmacologic treatments with some support (like exercise and mindfulness techniques).
- Includes no discussion of pharmacotherapy options, given that all prescribing for stimulant use disorders is done off label (that is, no Food and Drug Administration [FDA]-approved medication for any stimulant use disorder currently exists).
- Expands the discussion of special populations with unique treatment needs to cover racial/ethnic minorities, women (including those who are pregnant), men who have sex with men (MSM), transgender and gender nonbinary community members, adolescents, people experiencing homelessness/unstable housing, rural populations, people involved with the criminal justice system, people taking opioid use disorder medication, people who inject drugs, people with or at risk for HIV/AIDS, people with or at risk for hepatitis, and individuals with co-occurring mental disorders.

The purpose of this TIP is to advance the understanding of treating the SUDs associated with the use of cocaine and MA and the misuse of prescription stimulants. This TIP is organized to guide behavioral health service providers, healthcare service providers, and other addiction and allied professionals sequentially through the primary components of proper identification and management of stimulant use disorders. The TIP is divided into seven chapters so that readers can easily find the material they need most. Below is a summary of the TIP's main points and brief summaries of the first six chapters. (The seventh chapter is a listing of resources.)

Overall Key Messages

Stimulant use disorders are a growing problem in the United States, with more than 5 million people age 12 and older reporting past-year cocaine use, nearly 2 million reporting MA use, and almost 5 million reporting prescription stimulant misuse in 2019. Stimulant-related overdose fatalities are also on the rise, with the incidence of stimulant-related deaths more than tripling between 2010 and 2017.

Stimulant use disorders have a powerful neurobiological basis that includes changes in brain chemistry and functioning that in turn help drive stimulant use behaviors. But stimulant use disorders also have a social and environmental component that clinicians need to consider in trying to understand patients' stimulant use behaviors, difficulties in achieving and maintaining abstinence, and potential unwillingness to engage in formal SUD treatment.

Healthcare providers need to understand the medical complications of stimulant use, their clinical signs and symptoms, and appropriate management approaches. Behavioral health service providers should learn to recognize the medical complications of stimulant use so they can make quick and successful referrals to medical treatment as needed.

Ample research supports the use of CM as the primary psychosocial treatment for stimulant use disorders. The lack of FDA-approved pharmacotherapies for stimulant use disorders makes it vital for clinicians to learn about and offer psychosocial interventions (e.g., CM, CBT) and other nonpharmacologic services that have empirical support (e.g., mindfulness practices, family/couples counseling, the Matrix model of treatment).

Clinicians should consider a variety of factors in assessing why people with stimulant use disorders have sought treatment and what their individual treatment needs are. Clinicians can make treatment engagement—as well as treatment completion—more likely by maximizing access; addressing treatment ambivalence; training staff on how to provide respectful, patient-centered services; developing a well-thought-out treatment plan; and using techniques that help patients initiate and maintain abstinence.

Certain populations may be at an increased risk for stimulant use or, once they start using stimulants, may be at higher risk for negative outcomes (like contracting HIV). **Such populations—including women, people living in rural areas, people of diverse racial/ethnic backgrounds, MSM, and people experiencing homelessness/housing instability—may benefit from targeted treatment engagement techniques, interventions, and monitoring approaches that are tailored to their unique needs and challenges.**

Content Overview

This TIP is divided into seven chapters designed to thoroughly cover all relevant aspects of stimulant use disorders.

Chapter 1: Introduction

This chapter provides a broad introduction to stimulant use disorders and trends in stimulant use in the United States. The chapter also describes the goals and scope of the TIP as well as its intended audiences.

In Chapter 1, readers will learn about:

- Current rates of stimulant use disorders and overdose in the United States, including overdose involving the combination of stimulants with synthetic opioids (e.g., fentanyl) or semisynthetic opioids (e.g., heroin).
- Recent trends that are making stimulant use more lethal, such as the use of stimulants in combination with opioids or the increasing purity and decreasing price of cocaine and MA.
- The ongoing unmet treatment needs of people with stimulant use disorders, as well as the need for efforts to improve treatment retention.
- Rates of prescription stimulant misuse and how prescribers can help combat diversion.
- Legislation and regulations relevant to patients with stimulant use disorders and behavioral health and healthcare service providers who work with them.

Chapter 2: How Stimulants Affect the Brain and Behavior

This chapter reviews the ways in which brain structures, functions, and neurochemistry are altered in the presence of stimulants. The chapter also looks at the role of these alterations in the development and persistence of a stimulant use disorder.

In Chapter 2, readers will learn that:

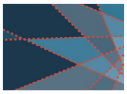
- Neurological reinforcement systems (i.e., the reward system, the stress system) and other brain structures and mechanisms underlie the occurrence of stimulant use disorders and influence key aspects of stimulant use disorders, like craving and memory dysfunction.
- Brain imaging technology has played an important role in helping researchers and clinicians understand the ways in which short- and long-term stimulant use can affect the brain.
- Stimulants alter the dopamine system in ways that can affect substance use. For instance, increased feelings of pleasure and euphoria when using a stimulant can reinforce its use.
- Providers should be aware of the specific medical and psychological acute and chronic effects of each of the three main types of stimulants generally used by individuals with stimulant use disorders: cocaine, MA, and prescription stimulant medication, such as methylphenidate for ADHD.

Chapter 3: Medical Aspects of Stimulant Use Disorders

This chapter describes medical and psychological signs, symptoms, and complications associated with stimulant use and stimulant use disorders and how to best manage common complications.

In Chapter 3, readers will learn that:

- The signs, symptoms, and harmful effects of stimulant use will vary depending on route of administration, dose, drug purity, level of intoxication, experience of withdrawal, chronicity, use history, and more.



- Medical complications of stimulant use can be serious and in some cases life threatening; these complications include cardiovascular disease, respiratory effects, cerebrovascular dysfunction, muscular and renal toxicity, gastrointestinal complaints, infections (including HIV), and hepatitis.
- Psychological complications include psychosis, aggression, and violence.
- People with stimulant use disorders often grapple with co-occurring disorders and conditions that can complicate diagnosis, treatment, and recovery. These disorders and conditions are secondary substance use (especially co-occurring opioid use), specific mental disorders (e.g., depression, anxiety, ADHD), medical conditions (e.g., dental problems, vein and nerve damage in the arm, cardiovascular disorders), and traumatic injury (e.g., due to violence/physical altercations).
- Patients' psychological reactions to stimulant use, like psychosis and violent behaviors, can also result in self-harm or harm to others if not managed properly.
- Coordinated care between medical and SUD treatment programs is a major aspect of properly identifying and treating co-occurring disorders and conditions of people with stimulant use disorders. Many patients will first appear for treatment or services in non-SUD settings—mainly primary care clinics and emergency departments.
- CM is by far the psychosocial treatment with the greatest scientific support. In some studies, CM is even more effective when used in combination with other psychosocial treatments, like community reinforcement.
- After CM, the three other psychosocial interventions with the most support are CBT, community reinforcement, and MI.
- Other forms of psychosocial treatment with less but still some support are the Matrix model, behavioral family or couples therapy, and case management/coordinated care.
- There is growing evidence that physical exercise, mindfulness, and transcranial magnetic stimulation also may help people with stimulant use disorders reduce their stimulant use or otherwise improve their health and well-being.
- Not all people with stimulant use disorders will be interested in formal SUD treatment. Offering harm reduction tools and strategies is critical because they can help people who continue to use stimulants stay alive. Harm reduction involves providing access to or information about:
 - Needle/syringe exchanges.
 - Fentanyl test strips (to determine whether drugs have been laced with fentanyl).
 - The opioid overdose reversal agent naloxone.
 - HIV prevention education.
- Rather than using a cookie-cutter approach to treatment selection (e.g., sending all patients to 60-day residential treatment), clinicians should consider each individual's unique SUD history and treatment needs and preferences. The American Society of Addiction Medicine's patient placement criteria can help guide the treatment selection process.

Chapter 4: Approaches to Treatment

This chapter describes the best supported nonpharmacologic approaches to helping patients begin and sustain recovery from stimulant use disorders.

In Chapter 4, readers will learn that:

- There are no FDA-approved medications for managing stimulant use disorders. This makes understanding available nonpharmacologic treatment options imperative.

Chapter 5: Practical Application of Treatment Strategies

This chapter briefly summarizes techniques clinicians can use to help engage patients in SUD treatment and maximize their chances of sustaining long-term recovery.

In Chapter 5, readers will learn that:

- People seek treatment for any number of reasons, and clinicians will better understand how to help their patients engage and stay in treatment if they know why their patients are entering treatment.
- Factors that can make treatment engagement more likely include:
 - Identifying barriers to treatment engagement.
 - Making treatment highly accessible.
 - Providing support for treatment participation.
 - Offering multiple treatment options.
 - Discussing with patients their expectations for treatment and any ambivalence they may have about treatment.
 - Working collaboratively with patients to develop a clear, flexible treatment framework.
- Staff should be educated about how to provide person-centered, respectful, empathic services, which can help encourage patients to stay engaged in treatment.
- To start treatment off “on the right foot,” clinicians should work with patients to set their treatment goals, fully assess their clinical needs, discuss reducing or discontinuing all substance use, and help them manage stimulant withdrawal symptoms.
- Treatment retention is critical. Simply put, people are less likely to die when in treatment than when not in treatment. Any amount of time people with stimulant use disorders remain in treatment is an opportunity for them to stay alive and improve their health.
- Many strategies can help patients maintain progress in recovery, such as teaching functional analysis of stimulant use; reinforcing positive behaviors with incentives; teaching strategies to avoid high-risk situations; offering relapse prevention techniques; and promoting connections to family, friends, and the community.
- Other services that can help patients maintain recovery are vocational counseling, social skills training, relationship counseling, mutual-help support programs, and wellness counseling. Clinicians should offer referrals for these services as needed.

Chapter 6: Treatment Considerations for Special Populations

This chapter discusses numerous populations that may be at increased risk for developing a stimulant use disorder or for experiencing negative outcomes associated with stimulant use (e.g., contracting HIV or hepatitis) and prescription stimulant misuse. These populations may require tailored assessment, treatments, or education to meet their unique needs and circumstances.

In Chapter 6, readers will learn that:

- Vulnerable populations are people of diverse racial/ethnic backgrounds, women (including those who are pregnant), MSM, transgender and gender nonbinary communities, adolescents, people experiencing homelessness/unstable housing, rural populations, people involved in the criminal justice system, people taking medication for opioid use disorder, people who inject drugs, people with or at risk for HIV/AIDS and hepatitis, and individuals with co-occurring mental disorders.
- Populations that experience health disparities related to systems of care and engagement in care may have higher rates of stimulant use disorder and increased issues accessing care for stimulant use disorders. They may also be more likely to experience secondary negative consequences related to these vulnerabilities (e.g., trauma or communicable diseases).
- By understanding the needs, SUD care access issues, and treatment considerations of these populations, clinicians will be more likely to provide patient-centered, effective care that maximizes rapport and treatment engagement.
- Services can be tailored to each of these populations to account for their unique risk factors, patterns of use, and health considerations. Clinicians may need to seek guidance from experts in these populations when tailoring treatment.

This page intentionally left blank.

TIP Development Participants

Note: The information given for participants in the TIP's development indicates their affiliations at the time of their participation and may not reflect their current affiliations.

Consensus Panel

Each Treatment Improvement Protocol's (TIP) consensus panel is a group of primarily nonfederal addiction-focused clinical, research, administrative, and recovery support experts with deep knowledge of the TIP's topic. With the Substance Abuse and Mental Health Services Administration's Knowledge Application Program team, members of the consensus panel develop each TIP via a consensus-driven, collaborative process that blends evidence-based, best, and promising practices with the panel members' expertise and combined wealth of experience.

Chair

Richard A. Rawson, Ph.D.
Executive Director
Matrix Center and Matrix Institute on Addiction
Deputy Director
UCLA Addiction Medicine Services
Los Angeles, CA

Workgroup Leaders

Felipe G. Castro, Ph.D., M.S.W.
Professor
Hispanic Research Center
Department of Psychology
Arizona State University
Tempe, AZ

James W. Cornish, M.D.
Assistant Professor of Psychiatry
Director
Division of Pharmacotherapy
Treatment Research Center
University of Pennsylvania
Department of Veterans Affairs Medical Center
Philadelphia, PA

Frances R. Levin, M.D.
Assistant Professor
Clinical and Educational Activities
Division on Substance Abuse
Columbia University
New York, NY

Michael J. McCann, M.A.
Research Coordinator
Matrix Center
Los Angeles, CA

Panelists

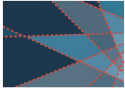
Arlene Hall, RN, M.S., CD
Director of Nursing
Hope House
Crownsville, MD

Stephen Higgins, Ph.D.
Professor
Departments of Psychiatry and Psychology
Ira Allen School
University of Vermont
Burlington, VT

Kyle M. Kampman, M.D.
Assistant Professor of Psychiatry
Treatment Research Center
University of Pennsylvania
Philadelphia, PA

Quintin Kingfisher
Medical Resources
Tribal Health
Lame Deer, MT

Judy Knobbe, M.S.W., LISW, CADC
Director
Heart of Iowa
Area Substance Abuse Council
Cedar Rapids, IA

**Wendy Lay**

Program Specialist
Bureau of Alcohol and Drug Abuse
State of Nevada
Carson City, NV

Scott M. Reiner, M.S., CAC, CCS

Substance Abuse Program Supervisor
Substance Abuse Services Unit
Virginia Department of Juvenile Justice
Richmond, VA

Ewa Szumotalska Stamper, Ph.D.

Police Psychologist
Honolulu Police Department
Private Practice, Clinical and Addictions Psychology
Honolulu, HI

Arnold M. Washton, Ph.D.

Private Practice of Addiction Psychology
Parkland, FL

Dennis A. Weis, M.D.

Medical Director
Powell Center for Disease Control
Iowa Lutheran Hospital
President, Iowa Chapter
American Society of Addiction Medicine
Des Moines, IA

Field Reviewers

Field reviewers represent each TIP's intended target audiences. They work in addiction, mental health, primary care, and adjacent fields. Their direct frontline experience related to the TIP's topic allows them to provide valuable input on a TIP's relevance, utility, accuracy, and accessibility. Additional advisors to this TIP include members of a resource panel and an editorial advisory board.

Original Field Reviewers

Patricia Bradford, LISW, LMFT, CTS

P.A. Bradford and Associates
Columbia, SC

Peter J. Cohen, M.D., J.D.

Special Expert
Medications Development Division
National Institute on Drug Abuse
National Institutes of Health
Bethesda, MD

Carol L. DeRosa, RN

Registered Nurse Consultant
Child Advocacy Unit
Anne Arundel County Department of Social Services
Severna Park, MD

Karen Kelly-Woodall, M.S., MAC, NCAC II

Criminal Justice Coordinator
Cork Institute
Georgia Addiction Technology Transfer Center
Morehouse School of Medicine
Atlanta, GA

Mitchell Markinem, M.A., NCAC II

Drug Court Program Coordinator
Fifth Circuit Solicitor's Office
Columbia, SC

Bonnie I. Pipe, B.S., CCDC

Clinical Director
Northern Cheyenne Recovery Center
Northern Cheyenne Board of Health
Lame Deer, MT

Lynda A. Price, Ph.D., ICADC

Treatment Coordinator
Global House
National Drug Commission
Hamilton, BD

Margaret M. Salinger, M.S.N., RN, CARN

National Nurses Society on Addiction
Department of Veterans Affairs Medical Center
Coatesville, PA

Richard E. Steinberg, M.S.

President
WestCare
Las Vegas, NV

Christopher J. Stock, Pharm.D.

Clinical Pharmacist
Substance Abuse Program
Veterans Medical Center
Salt Lake City, UT

Richard T. Suchinsky, M.D.

Associate Director for Addictive Disorders and
Psychiatric Rehabilitation
Department of Veterans Affairs
Mental Health and Behavioral Sciences Services
Washington, DC

Sushma Taylor, Ph.D.

Executive Director
Administrative Office
Center Point, Inc.
San Rafael, CA

Elizabeth Wells, Ph.D.

Research Associate Professor
Department of Psychiatry and Behavioral Sciences
University of Washington
Seattle, WA

2021 Update Field Reviewers**Justin Alves, RN, MSN, ACRN, CARN, CNE**

Addiction Nurse Educator
Office-Based Addiction Treatment Training and
Technical Assistance
Boston Medical Center
Clinical Instructor, Public Health
Northeastern University
Boston, MA

Amelia M. Arria, Ph.D.

Professor
Department of Behavioral and Community Health
Director
Center on Young Adult Health and Development
University of Maryland School of Public Health
College Park, MD

Wanda Barnett, M.S.

Primary Therapist – Addiction/Co-Occurring
Disorders
Retreat at Lancaster County
Retreat Behavioral Health
Ephrata, PA

Adam D. Bloom, M.S., LCPC, LPC, NCC, MAC

Clinical Director
Kolmac Outpatient Recovery Centers
Burtonsville, MD

Lucy R. Cannon, Ed.D., M.S.W., LCSW, LICSW, CCDP-D, MATS

Owner/Chief Executive Officer
LEJ Behavioral Health Services, LLC
Redan, GA
Adjunct Professor
Clark Atlanta University
Atlanta, GA

Mark Depman, M.D.

Attending Physician
Department of Emergency Medicine
Central Vermont Medical Center – University of
Vermont Health Network
Berlin, VT

Thomas E. Freese, Ph.D.

Co-Director
UCLA Integrated Substance Abuse Programs
Adjunct Professor
UCLA David Geffen School of Medicine
Los Angeles, CA

Peggy J. Gemperline, RN, B.S.N., M.B.A.

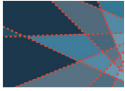
Vice President of Residential and Ambulatory
Services
Pinnacle Treatment Centers
Mt. Laurel, NJ

Amy Jeppesen, M.S.W., LCSW, ACADC

Behavioral Health Director Idaho/Iowa
Trivium Life Services
Adjunct Faculty
Boise State University
Boise, ID

Philip T. McCabe, CSW, CAS, CDVC, DRCC

President, NALGAP
The Association of Lesbian, Gay, Bisexual,
Transgender Addiction Professionals and their
Allies
Health Educator
Center for Public Health Workforce Development
Rutgers School of Public Health
Piscataway, NJ

**Mary McCarty-Arias, M.A.**

Rehabilitation Counselor and Trainer
Northeast Caribbean Addiction Treatment and Transfer Center
New York State Psychiatric Institute
Department of Psychiatry
Columbia University Medical Center
New York, NY

Larissa Mooney, M.D.

Director
University of California, Los Angeles
Addiction Psychiatry Division
Associate Professor of Psychiatry
University of California Los Angeles
Los Angeles, CA

Diana Padilla, RCR, CASAC-T

Research Project Manager
Northeast Caribbean Addiction Treatment and Transfer Center
Division on Substance Use Disorders, New York State Psychiatric Institute
Department of Psychiatry
Columbia University Medical Center
New York, NY

Jacynth (Jass) Pelland, M.S.W., LCSW, ACSW, LCADC, CJC

Program Coordinator
Intensive Recovery Treatment Support (IRTS)
Rutgers University Behavioral Health Center—Community Based Services
Rutgers School of Public Health
Piscataway, NJ

Saverio (Sam) Pirozzi, Ed.D., Ed.S., LMFT, LCADC, LPC

Private Practitioner & Consultant/Trainer
Stanhope, NJ, and Myrtle Beach, SC

John M. Roll, Ph.D.

Professor and Vice Dean of Research
Elson S. Floyd College of Medicine and College of Nursing
Washington State University
Spokane, WA

Kenneth Andrew Saffier, M.D.

President
Medical Education & Research Foundation for the Treatment of Addiction
Medical Director
National Coalition Against Prescription Drug Abuse
Medical Director
Bi-Bett, Inc.
Independent contractor/consultant
UCLA Integrated Substance Abuse Programs
University of California Los Angeles
Los Angeles, CA

Lisa L. Weyandt, Ph.D.

Licensed Psychologist
Director, Interdisciplinary Neuroscience Program
Professor, Department of Psychology
University of Rhode Island
Kingston, RI

Resource Panel

Patrick Carpenter

Policy Analyst
Executive Office of the President
Office of National Drug Control Policy
Washington, DC

Johanna Clevenger, M.D.

Chief
Alcoholism and Substance Abuse Program Branch
Indian Health Service
Rockville, MD

Peter J. Cohen, M.D., J.D.

Special Expert
Medications Development Division
National Institute on Drug Abuse
National Institutes of Health
Bethesda, MD

Jerome Jaffe, M.D.

Director
Office of Evaluation, Scientific Analysis and Synthesis
Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services Administration
Rockville, MD

George Kanuck

Office of Policy Coordination and Planning
Center for Substance Abuse Treatment
Substance Abuse and Mental Health Services
Administration
Rockville, MD

Kate Malliarakis, CNP, M.S.M., NCADC II

Executive Office of the President
Office for Demand Reduction
Office of National Drug Control Policy
Washington, DC

Eleanor Sargent, CAC, NCAC, M.A.

Director
Clinical Issues
NAADAC, The Association for Addiction
Professionals
Arlington, VA

Editorial Advisory Board**Karen Allen, Ph.D., RN, CARN**

Professor and Chair
Department of Nursing
Andrews University
Berrien Springs, MI

Richard L. Brown, M.D., M.P.H.

Associate Professor
Department of Family Medicine
University of Wisconsin School of Medicine
Madison, WI

Dorynne Czechowicz, M.D.

Associate Director
Medical/Professional Affairs
Treatment Research Branch
Division of Clinical and Services Research
National Institute on Drug Abuse
National Institutes of Health
Rockville, MD

Linda S. Foley, M.A.

Former Director
Project for Addiction Counselor Training
National Association of State Alcohol and Drug
Abuse Directors
Washington, DC

Wayde A. Glover, M.I.S., NCAC II

Director
Commonwealth Addictions Consultants and
Trainers
Richmond, VA

Pedro J. Greer, M.D.

Assistant Dean for Homeless Education
University of Miami School of Medicine
Miami, FL

Thomas W. Hester, M.D.

Former State Director
Substance Abuse Services
Division of Mental Health, Mental Retardation and
Substance Abuse
Georgia Department of Human Resources
Atlanta, GA

James G. (Gil) Hill, Ph.D.

Director
Office of Substance Abuse
American Psychological Association
Washington, DC

Douglas B. Kamerow, M.D., M.P.H.

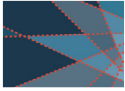
Director
Office of the Forum for Quality and Effectiveness in
Health Care
Agency for Healthcare Research and Quality
Rockville, MD

Stephen W. Long

Director
Office of Policy Analysis
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health
Rockville, MD

Richard A. Rawson, Ph.D.

Executive Director
Matrix Center and Matrix Institute on Addiction
Deputy Director
UCLA Addiction Medicine Services
Los Angeles, CA

**Ellen A. Renz, Ph.D.**

Former Vice President of Clinical Systems
MEDCO Behavioral Care Corporation
Kamuela, HI

Richard K. Ries, M.D.

Director and Associate Professor
Outpatient Mental Health Services and Dual
Disorder Programs
Harborview Medical Center
Seattle, WA

Sidney H. Schnoll, M.D., Ph.D.

Chairman
Division of Substance Abuse Medicine
Medical College of Virginia
Richmond, VA

Publication Information

Acknowledgments

This publication was prepared under contract numbers 270-95-0013 and 283-17-4901 by the Knowledge Application Program (KAP) for the Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration (SAMHSA), U.S. Department of Health and Human Services (HHS). Sandra Clunies, M.S., ICADC, served as the Contracting Officer's Representative (COR) for initial TIP development. Suzanne Wise served as the COR, and Robert Baillieu, M.D., M.P.H., as the Project Champion, for the TIP update.

Disclaimer

The views, opinions, and content expressed herein are the views of the consensus panel members and do not necessarily reflect the official position of SAMHSA or HHS. No official support of or endorsement by SAMHSA or HHS for these opinions or for the instruments or resources described is intended or should be inferred. The guidelines presented should not be considered substitutes for individualized client care and treatment decisions.

Public Domain Notice

All materials appearing in this volume except those taken directly from copyrighted sources are in the public domain and may be reproduced or copied without permission from SAMHSA or the authors. Citation of the source is appreciated. However, this publication may not be reproduced or distributed for a fee without the specific, written authorization of the Office of Communications, SAMHSA, HHS.

Electronic Access and Copies of Publication

This publication may be ordered or downloaded from SAMHSA's Publications and Digital Products webpage at store.samhsa.gov. Or, please call SAMHSA at 1-877-SAMHSA-7 (1-877-726-4727) (English and Español).

Recommended Citation

Substance Abuse and Mental Health Services Administration. *Treatment for Stimulant Use Disorders*. Treatment Improvement Protocol (TIP) Series 33. SAMHSA Publication No. PEP21-02-01-004. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2021.

Originating Office

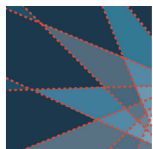
Office of Program Analysis and Coordination, Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, 5600 Fishers Lane, Rockville, MD 20857.

Nondiscrimination Notice

SAMHSA complies with applicable federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. SAMHSA cumple con las leyes federales de derechos civiles aplicables y no discrimina por motivos de raza, color, nacionalidad, edad, discapacidad, o sexo.

SAMHSA Publication No. PEP21-02-01-004
First printed 1999
Updated 2021

This page intentionally left blank.



Chapter 1—Introduction

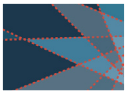
KEY MESSAGES

- Stimulant use disorders are a major public health concern in the United States, with more than 5 million people age 12 and older reporting past-year cocaine use, nearly 2 million reporting methamphetamine use, and almost 5 million reporting prescription stimulant misuse in 2019.
- Overdose deaths from stimulants have been increasing over the past 20 years, especially deaths attributable to stimulants taken with either synthetic opioids (e.g., fentanyl) or semisynthetic opioids (e.g., heroin). This underscores the importance of (1) having behavioral health and healthcare service providers understand and educate patients about the dangers of stimulant use disorders and (2) creating easy access to screening and treatment.
- Effective treatments for stimulant use disorders are available, but more behavioral health and healthcare service providers need to learn about these treatments and understand how and why to offer them to patients.

Chapter 1 of this Treatment Improvement Protocol (TIP) lays the groundwork for understanding the scope and effects of stimulant use disorders in the United States. The TIP generally uses the plural term “stimulant use disorders”—rather than the singular term “stimulant use disorder” found in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association [APA], 2013)—to reflect that patients may well misuse multiple substances classified as stimulants, including nonprescription stimulants. The plural term also conveys the purpose of this TIP—helping clinicians combat stimulant use and stimulant-related problems. This chapter will benefit all behavioral health and healthcare service providers who encounter patients with stimulant use disorders by giving a broad overview of why stimulant use disorders are so harmful and how information in this TIP can be leveraged to bring about more timely and effective management of these disorders.

Purpose of the TIP

Major U.S. institutions responded slowly to the dangers of stimulants throughout the 1970s and 1980s, partly because researchers and clinicians had only a partial picture of the basic biologic and psychological effects of these powerful psychostimulants. Knowledge gained over the past four decades about the properties of these substances can help clinicians understand, prevent, and treat the problems created by the use of cocaine and methamphetamine (MA) and the misuse of prescription stimulant medications (e.g., methylphenidate). This TIP summarizes the latest research as well as firsthand clinical experience of substance use disorder (SUD) treatment professionals.



Since the mid-1980s, there has been an explosion of knowledge about the effects of stimulants. Because these psychostimulants alter the functioning of the body and the brain, physicians and physician assistants, nurses and nurse practitioners, psychologists, social workers, licensed professional counselors, marriage and family counselors, SUD counselors, other behavioral health service providers, and peer recovery support specialists must understand the biologic aspects of stimulant use disorders. New areas of expertise include pharmacology, genomics, neurobiology, psychiatric and psychological manifestations, and treatment approaches for stimulant use disorders.

Stimulant use disorders do more than harm the people who have them. They can also negatively affect the lives of these individuals' family members, friends, neighbors, and coworkers. This wider effect makes it all the more important to help individuals with stimulant use disorders engage in SUD treatments and services.

This TIP presents current knowledge about the nature and treatment of stimulant use disorders. Because the Food and Drug Administration (FDA) has to date not approved any medications for stimulant use disorders, this TIP does not discuss pharmacology as a treatment strategy. The TIP is designed to provide scientifically established information about the effects of stimulants in a manner that makes it available and relevant for frontline treatment providers. In addition, the document reviews what is known about treating the medical, psychiatric, and SUD problems associated with the use of cocaine and MA and misuse of prescription stimulants. The treatment section emphasizes those approaches that have empirical support.

Organization of the TIP

This TIP opens with a broad overview of the current state of stimulant use disorders in the United States (Chapter 1) and then moves into the neurobiologic aspects (Chapter 2), assessment and diagnosis (Chapter 2), and medical management (Chapter 3) of stimulant use disorders. Chapter 4 introduces readers to empirically supported nonpharmacologic treatments for stimulant use disorders, and Chapter 5 takes an in-depth look at important clinical factors affecting the full continuum of care, including treatment initiation and abstinence maintenance. Chapter 6 discusses stimulant use among a range of special populations and specific considerations to improve engagement and treatment for the described populations. Finally, Chapter 7 provides a compendium of resources, including links to online information and tools.

Exhibit 1.1 defines important terms used in this publication. Also, note that the term “clinician” covers all healthcare providers and behavioral health service providers who work with people with stimulant use disorders and other SUDs. This could include psychologists, psychiatrists, national certified addiction counselors, licensed alcohol and drug counselors, marriage and family therapists, social workers, licensed professional counselors, physicians, nurses, and advanced practice healthcare providers (e.g., nurse practitioners, physician assistants). However, this term does not refer to peer recovery support specialists. Also, the TIP uses the term “patients” rather than “clients” or “consumers” to refer to people who are receiving any preventive services or care for stimulant use disorders or related conditions.

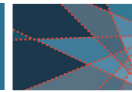
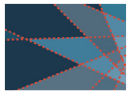


EXHIBIT 1.1. Key Terms

- **Craving:** A powerful desire for drugs.
- **Designer drug:** A synthetic analog of a restricted drug; has psychoactive properties.
- **Drug diversion:** The illegal distribution or use of prescription drugs or their use for purposes not intended by the prescriber (Centers for Medicare & Medicaid Services, 2016).
- **Physical dependence:** An adaptive physiological state that occurs with regular drug use and results in a withdrawal syndrome when drug use stops.
- **Stimulant use disorder:** According to DSM-5 (APA, 2013), a diagnosis based on the occurrence of at least two of the following criteria within a 12-month period (or 12 months before incarceration): (1) taking more of the stimulant than intended; (2) failing to reduce or control stimulant use, despite a wish or efforts to do so; (3) devoting excessive amounts of time to activities related to stimulant use; (4) having cravings or urges for the stimulant; (5) not meeting obligations at home, school, or work; (6) continuing to take stimulants, even if this use has led to or increased relationship or social difficulties; (7) forgoing or limiting important recreational, social, or job-related activities because of stimulant use; (8) taking stimulants in situations where doing so is physically hazardous; (9) continuing to take stimulants despite the realization that doing so has probably caused or aggravated a physical or psychological problem; (10) developing tolerance to the stimulants; and (11) experiencing withdrawal symptoms when stimulants are not taken or taking stimulants to ease or prevent withdrawal symptoms (Substance Abuse and Mental Health Services Administration, 2020m).
- This TIP uses the terms **amphetamine use disorder**, **cocaine use disorder**, and **methamphetamine use disorder** (or **MA use disorder**). Although these terms do not appear in DSM-5, they are used in research and survey literature. (Amphetamine use disorder and cocaine use disorder were classified as separate disorders in the previous edition of DSM.)
- **Substance misuse*:** The use of any substance in a manner, situation, amount, or frequency that can cause harm to users or to those around them. In the case of prescription medications, misuse is any use other than as prescribed or directed by a healthcare professional. For some substances or individuals, any use would constitute misuse (e.g., injection drug use).
- **Substance use disorder (SUD)*:** A medical illness caused by repeated misuse of a substance or substances. According to DSM-5 (APA, 2013), SUDs are characterized by clinically significant impairments in health and social function and by impaired control over substance use. They are diagnosed through assessing cognitive, behavioral, and psychological symptoms. SUDs range from mild to severe and from temporary to chronic. They typically develop gradually over time with repeated misuse, leading to changes in brain circuits governing incentive salience (the ability of substance-associated cues to trigger substance seeking), reward, stress, and executive functions like decision making and self-control. DSM-5 notes that both amphetamine-type and cocaine-type stimulant use disorders can develop as quickly as 1 week (APA, 2013). Multiple factors influence whether and how rapidly a person will develop an SUD, including the substance itself; the genetic vulnerability of the user; and the amount, frequency, and duration of the misuse.
- **Tolerance:** A condition in which higher doses of a drug are required to produce the same effect as experienced initially; often leads to physical dependence.
- **Withdrawal:** A psychological and/or physical syndrome caused by the abrupt cessation of the use of a drug in an habituated individual.
- **Withdrawal management:** A process of allowing the body to clear a drug while the symptoms of withdrawal are managed; often the first step in an SUD treatment program.

* Definitions of all terms with an asterisk correspond closely to those in *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*. This resource provides a great deal of useful information about substance misuse and its impact on U.S. public health. The report is available online (<https://addiction.surgeongeneral.gov>).



Scope of the TIP

This TIP looks at stimulants derived from the coca plant (cocaine hydrochloride and its derivatives) and the synthetically produced amphetamines. Regarding amphetamines, the TIP focuses on MA—the major illicitly produced and misused drug in this group—in its various forms. Certainly, there are other stimulants that are more widely used (e.g., caffeine) or that produce major health and social problems (e.g., nicotine); however, discussion of these substances is beyond the scope of this document.

Although considered drugs of misuse, MA analogs are not included in this document. These analogs are compounds with MA-like molecular structures but not necessarily effects similar to MA. Sometimes called designer drugs, they include MDA (3,4-methylenedioxy-amphetamine) and MDMA (3,4-methylene-dioxymethamphetamine).

Current Stimulant Use in the United States

Stimulant epidemics of the 1980s and 1990s had a devastating impact on American society. The impact of illicit stimulant use affected international politics, the U.S. legal system, and the U.S. healthcare system.

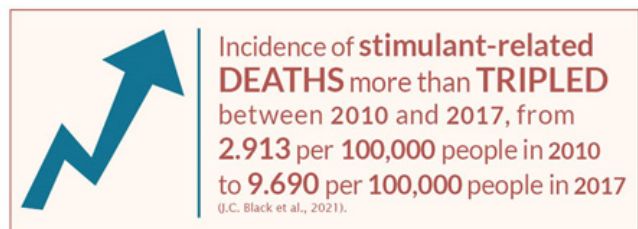
As the end of the 20th century neared, the powerful psychostimulants cocaine and MA and their derivatives joined opioids and alcohol as primary targets in the efforts to combat SUDs and misuse of prescription stimulants. The pressing need to effectively address the stimulant epidemic and treat people with stimulant use disorders produced a tremendous amount of scientific and clinical research. The results of this research broadened our knowledge of the human brain and expanded our understanding of SUDs.

Recent statistics demonstrate the scope of stimulant use in the United States. For instance (Center for Behavioral Health Statistics and Quality [CBHSQ], 2020a):

- Among people age 26 and older, past-month cocaine use increased slightly from 1.3 million in 2016 to 1.5 million in 2017, and essentially remained level for the next 2 years.
- Past-year MA use among people ages 18 to 25 increased moderately from 2016 to 2017 (approximately 256,000 to 375,000), but then leveled out around 275,000 in 2018 and 2019.
- Past-year MA use among people age 26 and older increased each year, from 1.1 million in 2016 to 1.7 million in 2019.
- Past-year prescription stimulant misuse was steady among people age 26 and older from 2016 to 2019. However, among people ages 18 to 25, misuse has decreased, from about 2.5 million in 2016 and 2017 to 2 million in 2019.

Stimulant-involved overdose deaths in the United States have skyrocketed over the past 20 years. From 1999 to 2019, overdose fatalities from psychostimulants with misuse potential other than cocaine (e.g., MA) grew more than 29-fold, from 547 deaths in 1999 to 16,167 in 2019 (National Center for Health Statistics [NCHS], 2020; National Institute on Drug Abuse [NIDA], 2021a). In that same time, overdose deaths due to cocaine increased from 3,822 in 1999 to 15,883 in 2019 (NCHS, 2020; NIDA, 2021a).

More recently, overdose deaths involving cocaine increased by 26.5 percent from the 12 months ending in June 2019 to the 12 months ending in May 2020. Overdose deaths involving other psychostimulants (e.g., methamphetamine, prescription stimulants, amphetamines) are provisionally calculated to have increased by 34.8 percent across the same comparison periods (Centers for Disease Control and Prevention [CDC], 2020c).



These patterns appear to be strongly driven by the increasingly popular trend of combining cocaine or MA with synthetic opioids (e.g., fentanyl) or nonsynthetic opioids (e.g., heroin). Most MA in the United States is cultivated and produced in Mexico, whereas Colombia is the United States' main supplier of cocaine (although the Mexico-Southwest border is the primary port of entry into the United States; Drug Enforcement Administration [DEA], 2019, 2021). Increasing amounts of the MA produced by Mexican cartels and transported into the United States now contain fentanyl in varying amounts. Much of the stimulant product sold on the street currently includes fentanyl.

Like MA, cocaine is increasingly being combined with fentanyl (or with both heroin and fentanyl, in what is known as a super speedball) to help offset the steep decline individuals experience when a cocaine "high" subsides (DEA, 2019, 2021). Most cocaine is adulterated with fentanyl at the "retail" level and not the "wholesale" level—that is, after it enters the United States (DEA, 2019, 2021).

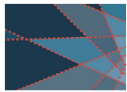
The connection of stimulant use to the opioid epidemic is very real and very dangerous:

- The State Unintentional Drug Overdose Reporting System found that, from January to June 2019, the most common stimulant in stimulant–opioid combinations leading to overdose death was cocaine (68.5% of cases), followed by MA (33.3%; O'Donnell et al., 2020).
- For both cocaine and MA, the number of overdose deaths also involving opioids has increased steadily since 2014. For cocaine, overdose deaths are primarily due to combinations with fentanyl or fentanyl analogs specifically (NIDA, 2021a).
- Data from the National Vital Statistics System found the percentage of cocaine-related overdose deaths also involving any opioid increased from almost 30 percent in 2000 to 63 percent in 2015 (McCall Jones et al., 2017).

Price and purity have likely played a role in the changing statistics on U.S. stimulant use, overdose, and fatalities. In 2018, the average purity of wholesale cocaine bricks analyzed by DEA's Cocaine Signature Program was 85 percent (DEA, 2019). In the first half of 2019, the average purity of MA was over 97 percent (DEA, 2021). From 2013 to 2017, the price of MA purchased in the United States decreased by more than 17 percent, from \$68 to \$56 per pure gram (DEA, 2019). Like MA, domestic purchases of cocaine also became less expensive from 2013 to 2017, falling from \$213 to \$153 per pure gram (DEA, 2019).

Also contributing to the increased lethality of MA is the shift toward production using phenyl-2-propanone as the chemical precursor to synthesis rather than ephedrine or pseudoephedrine. Using pseudoephedrine has been hindered somewhat by reduced access to sales of the over-the-counter product as a result of the Combat Methamphetamine Act of 2005 (see the text box "Legislative and Regulatory Milestones Since 2000"). The phenyl-2-propanone method bypasses the use of strictly controlled chemicals (i.e., ephedrine, pseudoephedrine) and yields a highly potent form of MA. More than 99 percent of MA samples analyzed in the first half of 2019 by the DEA Methamphetamine Profiling Program were manufactured using the phenyl-2-propanone method (DEA, 2021).

The breakdown of stimulant overdose patterns by race/ethnicity underscores differential effects among people of color. In 2019, the highest total number of psychostimulant-related deaths by race occurred among Whites (13,987), but the highest crude death rate by race was among American Indian/Alaska Native populations, at 8.1 deaths per 100,000 people (NCHS, 2020). (Crude death rates are a measure of the number of deaths within a given population during a specified period.) For cocaine, the highest crude death rate by race was among Blacks/African Americans, at 10.9 deaths per 100,000 people—more than twice that of the next-highest crude death rate (4.3 deaths per 100,000 Whites) and more than 4 times that of American Indian/Alaska Native populations (2.5 deaths per 100,000; NCHS, 2020).



ANNUAL HOSPITAL COSTS related to amphetamines **INCREASED NEARLY 500%** between 2003 and 2015—from **\$436 million to \$2.17 billion** (Winkelman et al., 2018).

Treatment for stimulant use disorders has been increasing recently. From 2015 to 2017, treatment admissions (i.e., the formal acceptance of a client into SUD treatment) for crack cocaine increased by 11 percent, for nonsmoked cocaine by 37 percent, for amphetamines by 41 percent, and for other stimulants by 62 percent (CBHSQ, 2020b).

But unmet treatment need is pervasive across SUDs broadly, with data from the Substance Abuse and Mental Health Services Administration's (SAMHSA) 2019 National Survey on Drug Use and Health indicating that only 10 percent of people age 12 and older who had a past-year SUD received any SUD treatment, and only 1 percent received treatment at an SUD specialty facility (CBHSQ, 2020a).

Treatment dropout is also a problem. A meta-analysis of 151 studies looking at SUD treatment rates (Lappan et al., 2020) found that the overall treatment dropout rate across all SUDs is 30.4 percent. By comparison, the treatment dropout rate is 53.5 percent for MA and 48.7 percent for cocaine (Lappan et al., 2020).

Cocaine

Both the increase in cultivation and production of cocaine from Colombia—which supplies more than 90 percent of U.S. cocaine seized by DEA—as well as the increased purity of cocaine entering the United States have made cocaine use, cocaine use disorder, and fatal overdose growing concerns over the past two decades (DEA, 2017; Kerridge et al., 2019). The prevalence of cocaine use among U.S. adults in 2019 was 5.5 million for past-year use, 2 million for past-month use, and 1 million for a stimulant use disorder involving cocaine (CBHSQ, 2020a).

The 2020 Monitoring the Future survey found that 2.9 percent of 12th graders reported past-year use of cocaine (University of Michigan, 2020). Cocaine use among adolescents and young adults is particularly worrisome given potential long-term effects on neurodevelopment, cardiovascular functioning, and psychosocial functioning, and the association between cocaine use and polysubstance use (Ryan, 2019).

In 2019, almost 65 percent of U.S. adults with cocaine use had a history of any mental illness, 36 percent had a serious mental illness, and 31 percent had at least one major depressive episode (CBHSQ, 2020a).

Methamphetamine

The prevalence of MA use among people age 12 and older in the United States in 2019 was 2 million for past-year use, 1.2 million for past-month use, and 1 million for a stimulant use disorder involving MA (CBHSQ, 2020a). From 2015 to 2018, approximately 1 million men and almost 600,000 women took part in past-year MA use (C. M. Jones et al., 2020). Of those adults with past-year MA use, 53 percent met criteria from the fourth edition of DSM for MA use disorder (C. M. Jones et al., 2020). The number of people age 26 and older with past-year MA use rose more than 50 percent from 2016 to 2019 (1.1 million in 2016 to 1.7 million in 2019; CBHSQ, 2020a).

MA use frequently co-occurs with other substance use and with a mental disorder (C. M. Jones et al., 2020). Among people 12 and older with past-year MA use in 2019, an estimated 68 percent engaged in past-year cannabis use, 43 percent in past-year opioid misuse, and 32 percent in past-year cocaine use; 24 percent experienced a past-year major depressive episode. Additionally, among adults who used MA in 2019, an estimated 27 percent had past-year serious mental illness (CBHSQ, 2020a).

Prescription Stimulant Misuse

Stimulant medication is FDA approved for treating attention deficit hyperactivity disorder (ADHD) and narcolepsy (a disorder of extreme sleepiness). Commonly prescribed stimulants include dextroamphetamine, dextroamphetamine/amphetamine combination product, and methylphenidate.

The prescribing of these medications has been increasing. National prescription stimulant dispensing rates grew significantly from 2014 to 2019, from 5.6 prescriptions per 100 persons to 6.1 per 100 persons, with the growth attributable in large part to increases among women and adults age 20 and older (Board et al., 2020). Total usage of prescription amphetamine, methylphenidate, lisdexamfetamine, and prescription MA, including extended-release formulations, doubled from 2006 to 2016 (Piper et al., 2018; Sembower et al., 2013). Further, from 2007 to 2011, the prevalence of children taking medication for ADHD increased by 28 percent, from 4.8 to 6.1 percent (Visser et al., 2014). Between 2013 and 2015, CDC reported a 344-percent increase in ADHD prescription medication claims by privately insured women ages 15 to 44 (K. N. Anderson et al., 2018).

Rates of nonmedical prescription stimulant use also are concerning. In 2019, almost 4.5 million adults in the United States reported past-year misuse, 1.4 million reported past-month misuse, and 492,000 met criteria for a stimulant use disorder involving prescription stimulant misuse (CBHSQ, 2020a).

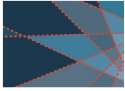
Data suggest diversion of stimulant medication is increasing among U.S. adolescents and may occur out of a desire to enhance academic performance (Colaneri et al., 2017). Additionally, among young adults, anywhere from 5 to 35 percent of college students reportedly misuse prescription stimulants not just for enhanced neurocognitive performance but for euphoric effects or weight control as well (Benson et al., 2015; Kilwein et al., 2016; Weyandt et al., 2013, 2016; Wilens et al., 2016).

Prescribers can help limit diversion of stimulants by adhering to DSM-5 criteria when diagnosing ADHD so that the medication is appropriately prescribed. When a prescription is written, the prescriber should cross-reference the prescription information with data available in state-run prescription drug monitoring programs. Prescribers can also help prevent stimulant medication misuse through numerous strategies, including (Colaneri et al., 2017):

- Using medication contracts.
- Educating patients, especially high school and college students who are diagnosed with ADHD, about the danger of sharing their medication with friends and the legal implications of this.
- Limiting prescriptions to a smaller number of pills.
- Implementing pill counts.
- Prescribing long-acting instead of immediate-release formulations.

Additionally, because overdiagnosis and incorrect diagnosis can lead to inappropriate prescribing, primary care providers should not diagnose ADHD themselves. Rather, they should refer patients to an appropriate mental health service professional (such as a psychiatrist or psychologist) for evaluation.

Prescribing nonstimulant medications for ADHD is another option that is particularly relevant for patients with a stimulant use disorder and co-occurring ADHD who want to pursue abstinence. Atomoxetine is a norepinephrine reuptake inhibitor that is not a DEA-controlled substance because it has very low misuse/stimulant use disorder potential (Clemow & Walker, 2014). Guanfacine and clonidine are alpha2-adrenergic receptor agonists that also have demonstrated good efficacy in reducing ADHD symptoms but have low misuse potential (Clemow & Walker, 2014). To learn more about managing ADHD in people with co-occurring stimulant use disorder, see Chapter 6.



LEGISLATIVE AND REGULATORY MILESTONES SINCE 2000

The statutory and regulatory landscape of SUD prevention and treatment has changed since the original publication of this TIP in 1999. Here are important statutory and regulatory developments related to the topics in this TIP:

- **The Drug Addiction Treatment Act of 2000:** This legislation, as amended, allows healthcare professionals who meet certain qualifications to offer Food and Drug Administration (FDA)-approved narcotic medication treatment for opioid use disorder in settings other than opioid treatment programs. (At the time of this publication, buprenorphine is the only approved medication that meets the provisions of the act.) This is relevant for patients with stimulant use disorder who are also using opioids and wish to initiate buprenorphine treatment. For the law as originally enacted, see Title XXXV here: www.govinfo.gov/content/pkg/PLAW-106publ310/pdf/PLAW-106publ310.pdf. For later statutory changes expanding buprenorphine prescribing, see www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines.
- **The Combat Methamphetamine Epidemic Act of 2005:** This act requires purchasers to show a photographic identification card or other acceptable document issued by a state or the federal government when buying over-the-counter cold medicines containing ingredients that are commonly used to make MA, such as pseudoephedrine. It also limits the amount of these products that can be purchased at one time and tracks purchasers. Read more about the act at www.deadiversion.usdoj.gov/meth/.
- **Fair Sentencing Act of 2010:** This act reduced the 5-to-10-year “mandatory minimum” prison sentence for possession of low-level crack cocaine. It also removed the mandatory minimum for simple possession of cocaine. Read more about the act at www.ussc.gov/research/congressional-reports/2015-report-congress-impact-fair-sentencing-act-2010.
- **The 21st Century Cures Act of 2016:** This act was passed to help increase the speed and efficiency of the discovery, development, and delivery of medical cures. It provided U.S. research and healthcare delivery institutions, like FDA and the National Institutes of Health, with funding to improve clinical trials, enhance data sharing, increase the recruitment of participants in clinical trials, and launch innovative research projects. It also established the State Targeted Response to the Opioid Crisis grant program. For the text of the act, see www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf.
- **The Comprehensive Addiction and Recovery Act (CARA) of 2016:** This legislation authorizes grant programs designed to expand SUD (especially opioid use disorder) prevention, education, treatment, and recovery efforts. The act includes provisions explicitly aimed at supporting such efforts in communities facing sudden increases in MA use. For the text of the act, see www.congress.gov/bill/114th-congress/senate-bill/524/text.
- **Confidentiality of Substance Use Disorder Patient Records (42 CFR Part 2):** Changes to these regulations—which pertain to patient records in federally assisted SUD treatment programs—were made in response to the opioid epidemic. For a summary of these revisions, review SAMHSA’s 42 CFR Part 2 Revised Rule Fact Sheet at www.hhs.gov/about/news/2020/07/13/fact-sheet-samhsa-42-cfr-part-2-revised-rule.html.

Importance of Science in Building Future Treatments

The original TIP's consensus panel believed that scientifically derived knowledge should serve as the foundation of treatment for stimulant use disorders. Findings from basic and clinical research efforts funded by NIDA, as well as other government and private institutions, have given treatment providers a set of strategies and tools to assist people with stimulant use disorders.

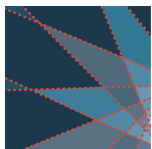
At this time, the approaches with the greatest empirical support combine psychosocial and behavioral strategies delivered in outpatient settings (e.g., contingency management, cognitive-behavioral therapy/relapse prevention). Emerging treatment techniques include exercise and mindfulness meditation. As knowledge of stimulants and brain functioning rapidly increases, thanks to active research funded by federal agencies and private foundations, other new approaches should soon be forthcoming. The development of pharmacotherapies for the treatment of stimulant use disorders remains a major priority of research efforts, and these efforts will likely provide some important new options in the near future.

Summary

Stimulant use and related deaths in the United States are growing problems that are intertwined with the current opioid epidemic. Stimulant use disorders have direct effects on the health and functioning of people with these disorders as well as secondary effects on others around them. This is partly what makes treatment so critical. SUD treatments and services not only help individuals with stimulant use disorders, but also benefit their entire support system and surrounding environment (e.g., family, friends, workplace, neighborhood). Treatment rates are lower than needed to keep pace with the number of individuals using stimulants and developing stimulant use disorders each year. New knowledge about how these substances influence the basic electrical and chemical activity of the human brain has allowed a better understanding of how and why stimulants affect human behavior, and this knowledge has rapidly influenced the development of new treatment efforts. This TIP provides an overview of:

1. The new knowledge about stimulants.
2. The treatment efforts to address stimulant use disorders.
3. Other clinical, medical, and social interventions developed in response to these disorders.

This page intentionally left blank.



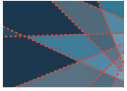
Chapter 2—How Stimulants Affect the Brain and Behavior

KEY MESSAGES

- A stimulant use disorder changes a person's brain in two major ways. One is neurotoxic (by affecting brain processes such as memory, learning, and other cognitive functions). The other way is by triggering the addiction process, such as by acting on the brain's reward system or through the development of craving. This information is critical for clinicians to understand because it explains the course of symptoms and recovery and underscores how difficult it is to quit using/misusing substances without interventions.
- A host of harmful effects can occur from acute and chronic cocaine or methamphetamine use, with some evidence from human studies suggesting that long-term stimulant exposure can cause persistent damage to the brain.
- The neurobiology of stimulant use disorders underscores the biologic aspects of substance use disorders as a chronic, relapsing medical illness. Understanding the changes in the brain that occur as someone becomes addicted to stimulants, experiences withdrawal, or stops using stimulants can also help guide clinicians in their approaches to treatment as well as help them understand behaviors and moods that a patient may experience throughout recovery.

Over the past several decades, research on substances of misuse has vastly improved understanding of human behavior and physiology and the nature of substance use disorders (SUDs). Basic neurobiologic research has enhanced understanding of the biologic and genetic causes of SUDs. These discoveries have helped establish SUD as a biologic brain disease that is chronic and relapsing in nature (National Institute on Drug Abuse [NIDA], 2018c; Volkow et al., 2019). By mapping the neural pathways of pleasure and pain through the human brain, investigators are beginning to understand how psychoactive substances, including stimulants, interact with various cells and neurochemicals in the brain.

This new information has also improved understanding of appropriate treatment approaches for different SUDs. This chapter describes the effects that acute and chronic cocaine and methamphetamine (MA) use, and prescription stimulant misuse, have on a person's brain and behavior. The chapter also discusses how to assess for and diagnose stimulant use disorders. Knowledge of the neurobiologic effects of stimulants will give clinicians greater insight into people who use stimulants, how to detect a stimulant use disorder in an individual, and why the treatment approaches described in Chapter 4 are effective.



Substance Use Disorders

SUDs are complex phenomena with numerous psychological, social, familial, emotional, and systemic contributors. SUDs often co-occur, and people with stimulant use disorders often also use or misuse other substances (Timko et al., 2018). However, at the core, SUDs involve a biologic process: the effects of repeated exposure to an agent (a substance) on a biologic substrate (the brain) over time (MacNicol, 2017; Volkow et al., 2019). Ultimately, adaptations that substance exposure elicits in individual neurons alter the functioning of those neurons, which in turn alters the functioning of the neural circuits and networks in which those neurons operate. This eventually leads to the complex phenomena that characterize SUDs (MacNicol, 2017).

Chronic substance use results in a complex set of physiological and neurologic adaptations. These adaptations are the body's attempt to adjust to or compensate for the intermittent or chronic presence of substances. Repeated exposure to a substance can also lead to adaptations in the reward circuitry that oppose and/or neutralize the substance's effects (i.e., counteradaptation). See Exhibit 2.1 for the parts of the brain that make up the reward circuitry. SUD-related brain activity can be characterized in three stages:

1. Acute intoxication/binge
2. Withdrawal/negative affect stage
3. Anticipation/craving

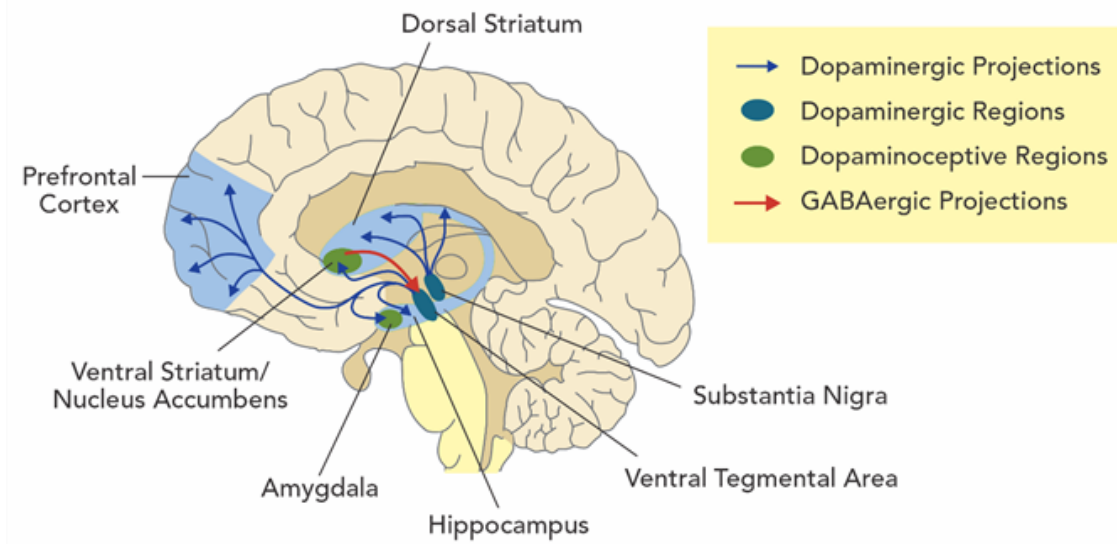
Each stage has its own complicated and intricate neurocircuitry that continues to reinforce the seeking and use of a specific substance (Koob & Volkow, 2016). There are more than 18 systems of neuromodulation involved in the perpetuation of the three stages of SUDs in the brain; three important structures and regions are the basal ganglia, the amygdala, and the prefrontal cortex (Koob & Volkow, 2016).

A SIMPLE WAY OF THINKING ABOUT SUDS

A helpful way to think about SUDs and the processes within the brain that go awry is to think of the brain as having a “stop” system and a “go” system (Office of the Surgeon General, 2016). The “go” system is the reward-seeking component that drives an individual to make decisions and achieve goals. The “stop” system inhibits the “go” system. In SUDs, the brain's “go” system is activated when an individual seeks substances in response to a substance-related cue in the environment. The “go” system also helps drive habitual behavior, which too can play a role in substance seeking. But the “stop” is ineffective in controlling these behaviors, because substance-related changes in the brain can decrease the “stop” system's activity and increase the “go” system's activity. Another way of thinking about this is that having an SUD is like driving a car without brakes (NIDAnews, 2014), which helps explain why people with SUDs cannot easily suppress their “go” system to “just stop” using or misusing substances.

With increasing use and development of tolerance to the effects of a substance, people will need to increase the amount taken to produce the desired effects. As substance use increases, so does disruption of executive function and of the reward and stress pathways. (The stress pathway comprises the various neurobiologic mechanisms invoked in response to stressful stimuli, such as the “fight or flight” response triggered by the hypothalamic–pituitary–adrenal axis.) These disruptions result in patients continuing to use and seek substances despite adverse consequences—the very definition of an SUD (Koob & Volkow, 2016).

EXHIBIT 2.1. Brain Structures Involved in the Reward System



Source: From Telzer (2016). Adapted with permission from Elsevier.

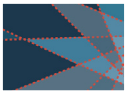
HOW TO UNDERSTAND A PERSON'S STRUGGLE WITH SUDS

Over the past three centuries, many theories evolved to explain why some people can use a substance with little risk, whereas others have difficulty controlling their use. The most widely accepted term for the combination of factors and processes contributing to the development of an SUD is **biopsychosocial**. This term includes the influence that genetic/biologic, psychological, and sociocultural factors have on short- and long-term effects of substance use. In the biopsychosocial model, all of these components are taken into account when working to prevent and treat SUDs (Skewes & González, 2013).

To understand the specific contribution of biology compared with the contribution of a person's environment, researchers look to monozygotic (i.e., identical) and dizygotic (i.e., nonidentical) twin studies. Twin studies often examine siblings who were separated at birth versus those who both remained in their family of origin. These studies point to the influence genes have on the development of SUDs (Ducci & Goldman, 2012). Although these genetic/biologic factors are clearly important, gender, development, environment, and culture also play a determining role.

Researchers' understanding of substance use is continually evolving and thus so are the models society uses to explain why some individuals can use substances without harm and others develop SUDs. The predominant model from the 18th and 19th centuries focused on morals. This "moral model" defined an SUD as a sin driven by the person's desires and wrongful choices. This model led to harsh treatment of people with SUDs, and its effects can still be seen in the stigma people with SUDs still encounter.

Continued on next page

*Continued*

Stigma and associated feelings of shame persist despite the fact that, by the mid-1900s, the disease model of SUDs had emerged, supported by research findings that there was no one type of person predisposed to alcohol use disorder. Additionally, advances in brain imaging allowed researchers to visualize neurologic changes in specific brain regions and neurotransmitters, highlighting the influence and primary importance of the reward systems involved.

These biologically driven findings led to the current understanding of SUDs as brain diseases, propelling clinical researchers to develop medicines to counter the physiologic effects on the brain (e.g., pharmacotherapies like methadone and naltrexone).

Although the basic neurologic structures are fairly consistent across humans, there is a considerable amount of neuroplasticity and researchers learned that the brain is both static and dynamic throughout the lifespan. In the 1970s, the social learning model emerged, highlighting the influence of social interactions and behaviors on SUDs (Giovazolias & Themeli, 2014). In this model, any person using a substance could become dependent through the influence of conditioning, modeling others, thinking about substance use, and still using despite the negative consequences.

An offshoot of the social learning model is the sociocultural model, which describes the effects of society on the individual's behaviors and takes into account differences across cultures, races, and ethnicities. This model aligns well with our newer understanding of social determinants of health, including food and housing insecurities, adverse childhood experiences, and generational trauma—all of which may be associated with more prevalent substance use.

Current SUD research suggests that clinicians and researchers need to take into account both physiologic components (e.g., genetics, neurobiology, neuroplasticity) and biopsychosocial aspects of the human experience (e.g., culture, environment and socialization, human development and behaviors throughout the lifespan) to develop a full conceptualization of the origin and severity of SUDs.

Neurobiology

The human nervous system is an elegant communication system, and the brain is the control center. The brain processes sensory information from throughout the body, guides muscle movement and locomotion, regulates a multitude of bodily functions, forms thoughts and feelings, modulates perception and moods, and essentially controls all behavior. Neurotransmitters (chemicals that transfer information between neurons and help neurons communicate with one another) also play a key role in the neurobiology of SUDs.

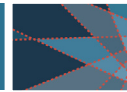
The Reward System or Positive Reinforcement

The brain circuit that is considered essential to neurologic reinforcement is called the **limbic reward system** (also called the **dopamine reward system** or the **brain reward system**).

This neural circuit extends across the **ventral tegmental area**, the **nucleus accumbens**, and the **prefrontal cortex**.

Substances of misuse—including stimulants—affect the reward system (Volkow et al., 2019). Normal functioning of the brain's circuitry results in inhibition and stimulation of neurotransmitters at multiple sites in the brain's reward systems. However, neuroadaptation and neuroplasticity that occur when substances are present can result in multiple neurotransmitters disrupting this normal circuitry, resulting in prolonged phases of withdrawal/negative affect and anticipation/craving (Koob & Volkow, 2016).

The neurotransmitter dopamine, which helps to regulate the feelings of pleasure (euphoria and satisfaction), is both directly and indirectly affected by stimulants (Volkow et al., 2019). Dopamine also



plays an important role in the control of movement, cognition, motivation, and reward (Bromberg-Martin et al., 2010; Volkow et al., 2019). In addition, stimulant use causes the brain to release norepinephrine, which helps regulate mood, attention, learning, memory, and arousal and may play a role in substance withdrawal (Office of the Surgeon General, 2016). The neurotransmitter serotonin affects reinforcement, motivation, learning, and memory, and may play a role in SUDs by making people more susceptible to compulsive (rather than controlled) substance use, especially people with genetic vulnerabilities to SUDs (Müller & Homberg, 2015).

Activities such as eating, drinking, and sex activate the reward system, inducing considerable communication among this structure's neurons. This internal communication leads to the release of dopamine. But substance use causes a surge of dopamine release that is far beyond that of natural activities, like eating and sex. The released dopamine produces immediate, but short-lived, feelings of pleasure and elation.

As dopamine levels subside, so do the feelings of pleasure. But if the activity is repeated, then dopamine is again released, and more feelings of pleasure and euphoria are produced. The release of dopamine and the resulting pleasurable feelings positively reinforce such activities and motivate the repetition of these activities. Moreover, with substance use, the person needs more and more of the substance to achieve the same level of pleasure.

Dopamine is believed to play an important role in the reinforcement of and motivation for repetitive actions (Daw & Tobler, 2013; Nutt et al., 2015; Volkow et al., 2019). An increasing amount of scientific evidence suggests that neuroadaptations to the reward and stress systems play a considerable role in the development of compulsive use behaviors (Koob & Volkow, 2016).

When the nucleus accumbens is functioning normally, communication among its neurons occurs in a consistent and predictable manner (Koob & Volkow, 2016). First, an electrical signal within a stimulated neuron reaches its point of connection

(i.e., the synapse) with the target (postsynaptic) neuron. The electrical signal in the transmitting (presynaptic) neuron triggers the release of dopamine into the synaptic gap (Koob & Volkow, 2016). Dopamine travels across the synaptic gap until it reaches the postsynaptic neuron. It then binds to the postsynaptic neuron's dopamine-specific receptors. The binding of dopamine to the receptor has an excitatory effect that generates an internal electrical signal within this neuron. However, not all of the released dopamine binds to the target neuron's receptors. Extra dopamine may be chemically deactivated, or it may be quickly reabsorbed by the presynaptic neuron through a system called the dopamine reuptake transporter (see Exhibit 2.2).

The postsynaptic neuron receives messages in the form of neurotransmitters released from the presynaptic neuron, resulting in depolarization or hyperpolarization of the postsynaptic neuron membrane. If the membrane is depolarized to a certain degree, an action potential occurs that causes the neuron to release a neurotransmitter (i.e., to "send a message").

To learn more about the reward circuit in stimulant use disorders, see the NIDA video "The Reward Circuit: How the Brain Responds to Cocaine" (<https://www.drugabuse.gov/videos/reward-circuit-how-brain-responds-to-cocaine>).

The Stress System or Negative Reinforcement

In addition to positive reinforcement through the brain's reward system, negative reinforcement can play a key role in the development and maintenance of chronic, compulsive substance use (Wise & Koob, 2014). The motivation to use a substance to avoid discomfort is an example of negative reinforcement. This motivation to continue using a substance occurs in the withdrawal/negative affect stage of substance use and also in the anticipation/craving stage.

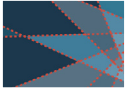
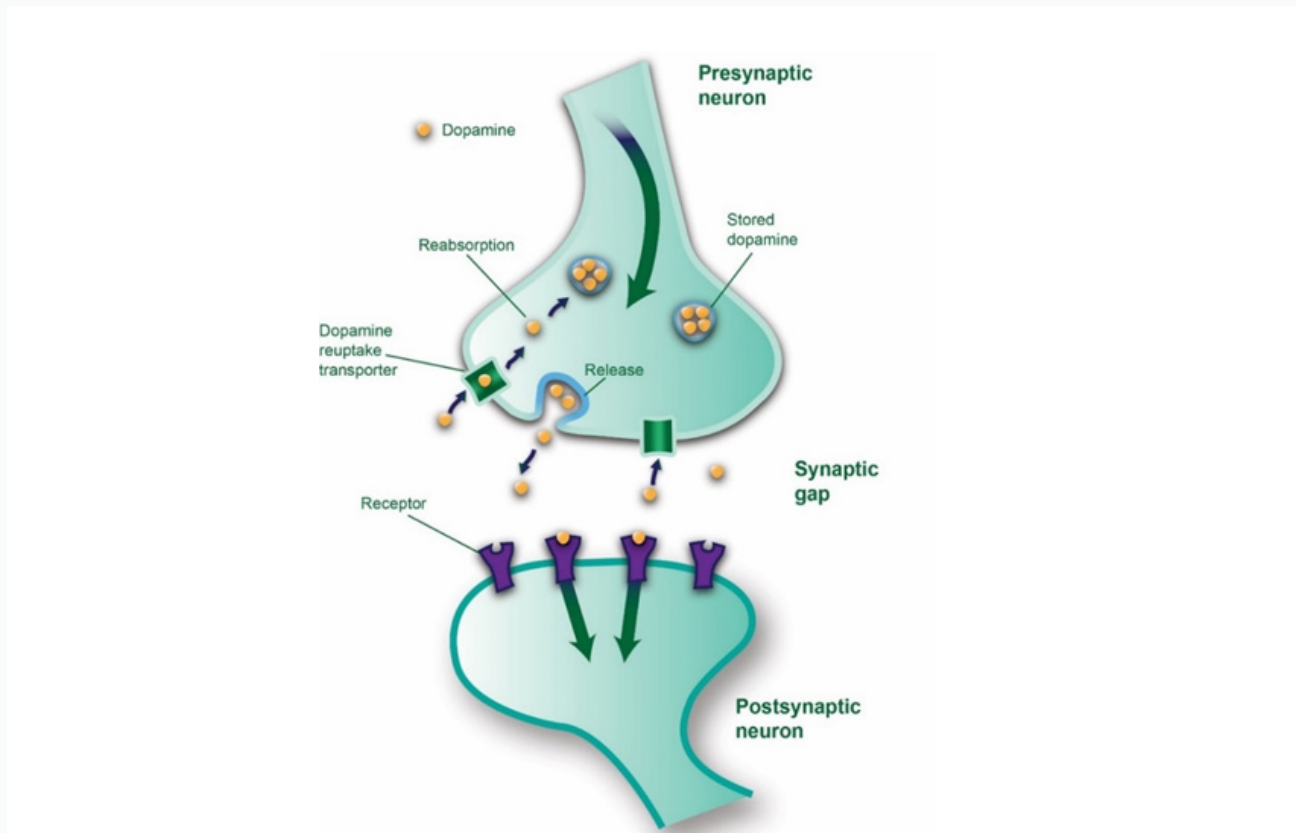


EXHIBIT 2.2. Normal Dopamine Transmission



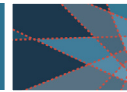
As people experience negative withdrawal symptoms from not using a substance, their brain circuitry causes further dysregulation of executive function and other cognitive processes. This dysregulation creates negative effects in the absence of the substance, further driving the precontemplation/craving phase to reinforce the compulsive seeking and taking of the substance (Koob & Volkow, 2016).

Experimental evidence supports the theory that stimulants and other commonly misused substances imitate, facilitate, or block the neurotransmitters (especially dopamine) involved in brain reinforcement systems (Ashok et al., 2017; dela Peña et al., 2015; Nutt et al., 2015; Volkow et al., 2019). Negative reinforcement

through overactivation of the stress system or the anti-reward system could also play a role in the perpetuation of chronic recurrent use to alleviate negative effects (Koob & Volkow, 2016).

Drug Craving and Memory

The degree to which learning and memory sustain the addictive process has also been addressed. Researchers believe that each time a neurotransmitter like dopamine floods across a synapse, circuits that trigger thoughts and memories and that motivate action become more strongly activated in the brain. Moreover, activation of the reward system creates a very powerful association between the euphoric and other rewarding effects of the substance and whatever



people, objects, or places the individual is exposed to at the time; these people, objects, or places then can become cues for substance use (Office of the Surgeon General, 2016).

Craving, a central aspect of SUDs, is a very strong learned response with powerful motivational properties often associated with specific memories (i.e., conditioned cues and triggers; Carmack et al., 2017). Cues—any stimuli (e.g., drug paraphernalia, moods, friends who use substances, locations associated with substance use) repeatedly paired with substance use over the course of a patient's SUD—can become so strongly associated with the substance's effects that the associated (conditioned) stimuli can later trigger arousal and an intense desire for the substance and lead to recurrent use (Carmack et al., 2017). High recurrence rates are common in people with stimulant use disorders even after treatment (Brecht & Herbeck, 2014).

Brain imaging studies have shown that cue-induced drug craving may be linked to distinct brain systems involved in memory (Moreno-Rius & Miquel, 2017; Perry et al., 2014). Brain structures involved in memory and learning, including the dorsolateral prefrontal cortex, amygdala, and cerebellum, have been linked to cue-induced craving (Moreno-Rius & Miquel, 2017; Sinha, 2013). A network of these brain regions integrates emotional and cognitive aspects of memory and triggers craving when it reacts to cues and memories. These cues and memories also play an important role in reinforcing substance use (Carmack et al., 2017). In contrast, negative experiences (e.g., violence, trauma, paranoia) that occur during acute intoxication do not seem to reinforce avoidance of intoxication.

Most SUD treatment approaches recognize the power of these factors in triggering recurrent use and warn patients to avoid everything previously associated with their substance use. Treatment approaches that address these learning and memory issues of SUDs may prove effective. For example, cue exposure therapy uses extinction (i.e., breaking the individual's association

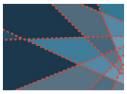
between the trigger or cue—like seeing drug paraphernalia—and the conditioned response—such as experiencing feelings of craving) to help decrease physiologic reactions to triggers and decrease cravings (Carmack et al., 2017; Torregrossa & Taylor, 2013).

Researchers have examined other methods of similarly reducing physiologic responses to triggers and thereby reducing craving, such as inhibiting memory reconsolidation (i.e., the process of stabilizing newly formed memories so they can be stored long term) and using pharmacologic agents (e.g., propranolol) to enhance the extinction process used in cue exposure therapy (Torregrossa & Taylor, 2013). People with SUDs may further benefit from cue exposure therapy that is combined with other psychosocial interventions, like cognitive therapy and motivational enhancement (Kaplan et al., 2011).

Role of Technologies

The development of noninvasive brain imaging (e.g., positron emission tomography [PET] scans) has created a powerful new tool for demonstrating not only the short-term effects of substance use but also the longer term consequences of chronic substance use and SUDs. These tools have allowed researchers to go where they previously could not—literally into a living human brain. However, this research is still maturing, and many questions remain about whether and how these technologies might inform clinicians' care of people with stimulant use disorders.

Such noninvasive techniques can depict higher or lower activity levels of different brain areas by measuring metabolic activity (e.g., glucose use; Fakhoury, 2014). They can identify substance-induced structural changes and physiologic adaptations (Fakhoury, 2014). Through a combination of techniques, researchers and clinicians can observe the altered processing of information in various circuits as the brain responds to substance use.



Using noninvasive imaging techniques, investigators have been able to identify brain structures involved in craving, map the emotions of people who use substances, and plot the neurobiologic basis of substance-induced euphoria. For example, researchers have used functional magnetic resonance imaging to predict substance use relapse and maintenance of abstinence (S. J. Moeller & Paulus, 2018). Additional neuroimaging studies have demonstrated significant changes in gray matter and in neurochemistry and have also predicted long-term effects of substance use and potential for recurrent use (S. J. Moeller & Paulus, 2018).

PET has revealed subtle alterations in the dopamine receptors in the brains of people who use stimulants (Solingapuram Sai et al., 2019). A review of some PET studies has demonstrated not just reductions in dopamine receptor availability and sensitivity associated with cocaine and MA use, but also increased dopamine release (Wiers et al., 2016). Combining PET with the radiotracer [^{18}F]-fluorodeoxyglucose—which is used to visualize brain glucose metabolism—has helped researchers understand changes in the brain’s metabolic activity associated with craving, alterations in cognition, self-regulation, and intoxication (Wiers et al., 2016).

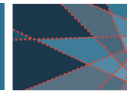
PET imaging has also provided insight into stimulant-related effects on neurofunction such as identifying inflammation in the brain, understanding the influence of cocaine on mu-opioid receptor binding, and pinpointing increases in norepinephrine in the synapses due to blockage of its reuptake (Wiers et al., 2016). Single photon emission computerized tomography—a form of PET that uses a different type of radiotracer—may prove to be a useful diagnostic and classification tool (e.g., differentiating people at high risk of recurrent use from those who are not).

Structural magnetic resonance imaging studies of people with MA use have shown clear gray matter deficits in cortical areas (i.e., frontal, insular, cingulate, temporal, and occipital cortices) and in the hippocampus, along with an increase

in volume in the parietal lobe and the striatum (Hall et al., 2015; Jan et al., 2012). White matter enhancement appears to occur in the temporal and occipital lobes, accompanied by widespread white matter hyperintensities and aberrations in the corpus callosum (Jan et al., 2012). Structural changes documented in people with cocaine and amphetamine use include reduced gray matter in the insula, ventromedial prefrontal cortex, inferior frontal gyrus, pregenual anterior cingulate gyrus, and anterior thalamus (Ersche et al., 2013; Hall et al., 2015). Research is ongoing to better understand what these patterns mean and how structural deficits and changes affect substance use behaviors and outcomes.

Imaging research is also providing important evidence about changes that can take place in the brain with abstinence and SUD treatment. For instance, exercise training for people in treatment for MA use disorder (and who were abstinent) was associated with recovery of certain striatal dopamine receptors that are known to become deficient with MA exposure—although it should be noted that abstinence plus education did not produce these benefits (C. L. Robertson et al., 2016). Nonetheless, such research suggests that healing in the brain can occur, providing additional evidence for the importance of promoting abstinence and recovery.

Although mapping brain activity during stimulant use and withdrawal may allow researchers to further document substance-induced neuropsychological impairments, not much of this research has been conducted in humans. Animal models suggest stimulant withdrawal is accompanied by a reduction in modularity—the ability of independent and functionally separate networks within the brain to interact with one another, somewhat like an electric circuit board with independent circuits that can connect to one another (Kalvar & Medaglia, 2018). Reduced modularity appears to occur in thalamic regions for MA and in a combination of midbrain-cortico-thalamic-hypothalamic-amygdalar brain regions for cocaine (Kimbrough et al., 2019).



The continuing development and application of new technologies such as noninvasive brain imaging will allow researchers to improve their understanding of how stimulants affect the human brain. Greater understanding of the underlying neuronal impairments of stimulant use will aid in the development of new and more effective treatment approaches.

Stimulant Use and the Brain

To better understand underlying drivers for substance use, it is important to learn the effects of any particular substance on a given person. For instance, someone with long-term stimulant use who is taking a stimulant and an opioid at the same time will be affected differently by that stimulant than someone taking a stimulant alone and for the first time. How stimulants affect individuals (both universal effects as well as person-specific effects) can provide helpful information to providers to assess, treat, and prevent recurrent use of the substance (Volkow et al., 2017).

Once a substance enters the bloodstream, it is transported throughout the body to various organs and organ systems, including the brain. To enter the brain, a substance's molecules must first get through its chemical protection system, which consists mainly of the blood–brain barrier. Tight cell-wall junctions and a layer of cells around the blood vessels keep large or electrically charged molecules from entering the brain. However, small neutral molecules like those of cocaine and MA easily pass through the blood–brain barrier and enter the brain (Kousik et al., 2012; Turowski & Kenny, 2015). Once inside the brain, substances begin to exert psychoactive effects.

Stimulants' Mechanisms of Action

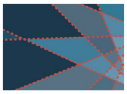
On a short-term basis, stimulants exert their effects by disrupting or modifying the normal communication that occurs among brain neurons and brain circuits. Cocaine and MA have both been shown to disrupt the dopamine neurotransmitter system—cocaine indirectly and MA both directly and indirectly (Ashok et al., 2017). Both cocaine and MA can inhibit the reuptake and release of dopamine by the presynaptic neuron, resulting in excess dopamine in the synaptic gap.

The two common forms of prescription stimulants—methylphenidate and amphetamine—affect the dopamine system differently, but, like cocaine and MA, both result in increased extracellular dopamine. Methylphenidate inhibits the reuptake of dopamine, as does amphetamine; but amphetamine also increases the amount of dopamine initially released into the synaptic gap (Yanofski, 2011).

Whereas the mechanism of action of prescription stimulants is not drastically different from that of cocaine and MA, differences in effects can occur based on who is taking the substance (e.g., someone with attention deficit hyperactivity disorder [ADHD] versus someone without it), the dose taken, and how it is administered. These differences influence whether the prescription stimulant is a helpful therapy or a drug that can change the brain at the cellular and structural levels. Specifically, if a person has ADHD and takes a prescription stimulant, the medication is provided at a dose that increases dopamine to a level that provides relief from ADHD. When taken as directed (i.e., orally at the prescribed dosage and according to schedule), it provides a constant blood level of the medication. People with ADHD will feel more focused and productive as a result. But when MA, cocaine, or prescription stimulants are injected or smoked (or, in the case of medications, taken in higher-than-prescribed amounts or taken by people without ADHD), they can lead to brain changes and stimulant use disorder.

The use of stimulants increases the amount of available dopamine in the brain (Paulus & Stewart, 2020). High levels of available dopamine in the brain generally enhance mood and increase body movement (i.e., motor activity) and motivation, but too much dopamine may produce symptoms that approximate positive symptoms of schizophrenia (e.g., delusions, hallucinations, paranoia; Kesby et al., 2018; Klein et al., 2019). With cocaine, the effects are generally short-lived, whereas with MA, the duration of effect is much longer.

As the stimulant level in the brain decreases, the dopamine levels subside to normal, and the pleasurable feelings dwindle. With repeated



stimulant use, dopamine stores in the brain become temporarily depleted (Ashok et al., 2017), resulting in the depressive and exhaustive symptoms associated with stimulant withdrawal.

Although the neurochemical pathways of chronic stimulant use disorders are not definitively established, a few researchers have found evidence of changes in the structure and function of brain neurons after chronic stimulant use in humans. Some researchers propose that the changes may come from dopamine depletion, changes in neurotransmitter receptors or other structures, or changes in cellular components or other brain messenger pathways that could cause the changes in mood, behavior (e.g., compulsivity, decision making), and cognitive function associated with chronic stimulant misuse (Ashok et al., 2017; Jan et al., 2012). (The medical aspects of stimulant use disorders are discussed in Chapter 3.)

General Effects of Stimulants

Stimulants affect the normal functioning of the dopamine neurotransmitter system (Volkow et al., 2019). Stimulants appear to increase the brain's levels of free dopamine (Ashok et al., 2017; dela Peña et al., 2015; MacNicol, 2017; Volkow et al., 2019). The higher the substance dose, the greater the individual's feelings of wakefulness, mania, and euphoria. As the dopamine levels and pleasurable feelings subside, the individual experiences an intense desire to replicate the feelings of pleasure by administering another dose of the substance. As with substance use generally, this tendency toward repeated administration is characteristic of stimulant use disorders and underlies most of the other effects of stimulants, as well as most other addictive substances.

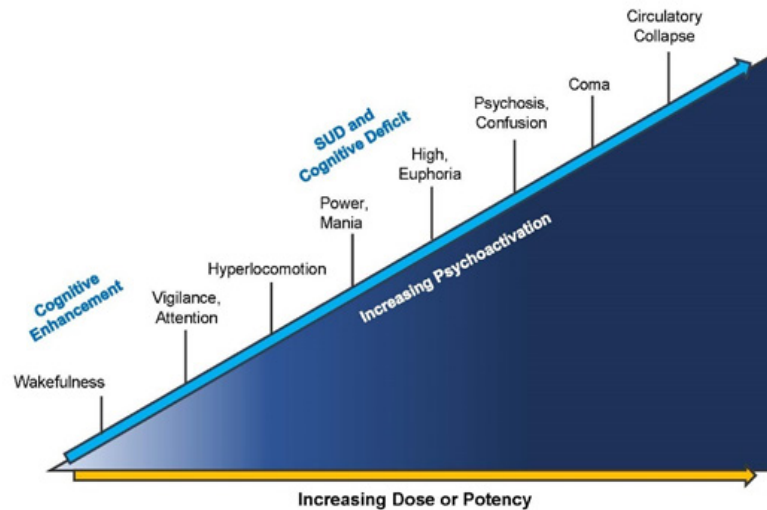
Half-lives of stimulants vary by drug. Cocaine, being naturally derived, has a much shorter half-life (around 60 minutes), whereas MA, being synthetic, has a half-life of around 10 hours (Coe et al., 2018; Cruickshank & Dyer, 2009). The half-lives of prescription stimulants also vary by drug and

by formulation (e.g., short-acting versus long-acting). For example, short-acting prescription amphetamine has a half-life of approximately 9 hours, whereas the long-acting formulation has a half-life in the range of 10 to 13 hours (Pradeep & Standeven, 2019).

Continued use often leads to adverse consequences, which may include neuropsychologic impairment, mental health issues, and diminished physical health. Work performance and social and family relations can be adversely affected, and the risk of arrest and criminal/legal involvement increases (McKetin et al., 2020).

It is important to note that in small and measured doses, stimulants may serve a clinical purpose to heighten wakefulness, help focus attention, and enhance cognition (see Exhibit 2.3). This could explain why some people who misuse prescription stimulants—especially adolescents in high school and young adults in college—often do so to improve their concentration and alertness, which they perceive as helping with their studying and academic performance (Clemow & Walker, 2014; Weyandt et al., 2018). Increasing doses, higher potency, and more frequent use increase psychostimulation and may eventually result in the cognitive impairments often correlated with stimulant use disorder (Wood et al., 2014). In very high doses, stimulant use can lead to serious medical complications, including coma and circulatory collapse, or even death (Wood et al., 2014).

For patients with a stimulant use disorder, impairments in the brain's reward systems that lead to problems with cognition and neuropsychiatric functioning may persist even after cessation of stimulant use (Taylor et al., 2013). Cravings for the stimulant's effects tend to linger, even after abstinence has been achieved, and the potential for recurrent use is high.

EXHIBIT 2.3. Continuum of Psychostimulant Activation

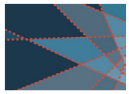
Increasing cognitive activation as stimulant dose increases initially produces increased wakefulness and cognitive enhancement. These are the beneficial effects. As dose or potency increases, a sense of power and euphoria can ensue. These are the effects people with SUD seek. Such effects are accompanied by cognitive deficits. Higher doses can result in overdose, psychosis, coma, and eventual circulatory collapse

Source: Wood et al. (2014). Adapted with permission.

Effects of Combining Psychostimulants With Opioids

Psychostimulant-related overdose deaths involving opioids have been increasing over the past 20 years, with heroin and synthetic opioids (like fentanyl) largely accounting for psychostimulant-associated fatalities since 2010 (McCall Jones et al., 2017). Polysubstance use, specifically the co-consumption of synthetic opioids and psychostimulants, like cocaine and MA, was largely responsible for the increases in cocaine- and MA-related overdose deaths observed from 2012 to 2017 (Kariisa et al., 2019).

Opioids can lead to potentially lethal respiratory depression. This is especially true of fentanyl and fentanyl analogs, which are rapid acting and are increasingly being taken in combination with cocaine or MA, by accident or on purpose (LaRue et al., 2019). Fentanyl can induce fatal respiratory depression in as little as 2 minutes (Kuczyńska et al., 2018). Even if nonfatal, respiratory depression is dangerous and can lead to hypoxic brain injury (Kiyatkin, 2019). Because people naïve to opioids lack opioid tolerance, they may be at an increased risk of unintentional overdose when combining stimulants, like cocaine, with fentanyl or other synthetic and nonsynthetic opioids (LaRue et al., 2019).



Effects of Route of Administration

The five most common routes of administering psychoactive (mood-changing) substances are:

- Oral consumption (i.e., swallowing, gumming [rubbing the substance on the gums]).
- Intranasal consumption (i.e., insufflation).
- Inhalation into the lungs (i.e., smoking).
- Intravenously (i.e., injection).
- Vaginal or anal insertion.

Cocaine and MA can be smoked, snorted, injected, ingested orally, or absorbed intrarectally or intravaginally. Prescription stimulants can be taken orally or crushed and snorted. The route of administration affects the amount (i.e., the dosage) of stimulant delivered to the brain, the speed at which it is delivered, and the resulting intensity of the stimulant's effects—which in turn may affect the course of an SUD. Because a person's preferred route of administration affects the extent and depth of chronic effects, it has implications for treatment decisions (see Chapter 5). (For specific information on drug use and peak effects, see Chapter 3, Exhibit 3.2.)

The long plateau effect and the much longer half-life of MA versus cocaine suggest considerable dangers in repeated use of MA (Cruickshank & Dyer, 2009). Because stimulants exert their effects in a dose-dependent manner, the route of administration has serious neurologic, physical, psychiatric, and neurocognitive implications for the person using the stimulant. Prolonged high doses of stimulants (e.g., during binges or chronic use) may cause greater and longer lasting neurologic damage, which in turn may lead to greater and longer lasting cognitive deficits.

The onset of stimulants' chronic effects varies across individuals, and although there are few data to predict how long it will take for any person to begin experiencing the chronic effects of stimulant use, onset is probably related to:

- The amount of stimulant used.
- The frequency of use.
- The route of administration.
- Significant medical comorbidities.
- Co-occurring mental disorders.
- Co-administration of other substances.

- The environment in which the substance is taken.
- Genetics and metabolic factors.

However, in general, higher, more frequent doses of stimulants used in combination with other substances result in more rapid transition to the effects of chronic stimulant exposure. (For a discussion of route-of-administration effects on toxicity and adverse reactions, see Chapter 3.)

Psychological and Neurocognitive Effects

The immediate psychological effects of stimulant administration include a heightened sense of well-being, euphoria, excitement, and alertness, and increases in motor activity, similar to what would be seen in a manic state. Stimulants also reduce appetite and may result in insomnia. Stimulants may also enhance focus and libido (Volkow et al., 2007).

High doses, particularly in the setting of sleep deprivation, may result in restlessness, agitation, and more profound psychiatric presentation, including altered perceptions of reality and hallucinations. Chronic psychological effects of stimulant use and withdrawal may include paranoia, psychosis, depression, and/or suicidal ideation.

Cocaine

Routes of Administration

Cocaine is most commonly taken by nasal insufflation (snorting), intravenous injection, or inhalation of smoke vapors (smoking/inhalation). Less often, it is taken orally, vaginally, rectally, or sublingually. The half-life of cocaine is about 60 minutes (Coe et al., 2018) but can range from 40 to 90 minutes (ARUP Laboratories, 2019).

Pharmacology

Cocaine has two main pharmacologic actions. It is both a local anesthetic and a central nervous system (CNS) stimulant (NIDA, 2016a). Cocaine exerts its local anesthetic actions by blocking the conduction of sensory impulses within nerve cells. This effect is most pronounced when cocaine is applied to the skin or to mucous membranes. Cocaine has approved medical use as a local anesthetic in some surgery of the eye, ear, and throat (NIDA, 2016a).

As a CNS stimulant, cocaine affects a number of neurotransmitter systems, but it is through its interaction with the dopamine and the limbic reward system that cocaine produces some of its most important effects, including positive reinforcing effects (NIDA, 2016a). The major influence of cocaine on the dopamine system is its ability to block the synaptic reuptake of dopamine.

Cocaine does not directly stimulate the dopamine system; rather, it causes the system to be stimulated by preventing dopamine from being removed from the synaptic gap. Cocaine's blockade of the dopamine reuptake transporter extends the availability of dopamine in the synaptic space, where it continues to occupy the dopamine receptors and causes the postsynaptic neurons to fire for a longer-than-normal period (NIDA, 2016a). (See Exhibit 2.4.)

Acute Physiologic Effects

Acute cocaine use can lead to narrowing of the blood vessels and an increase in body temperature, pulse, and blood pressure (NIDA, 2016a) as well as

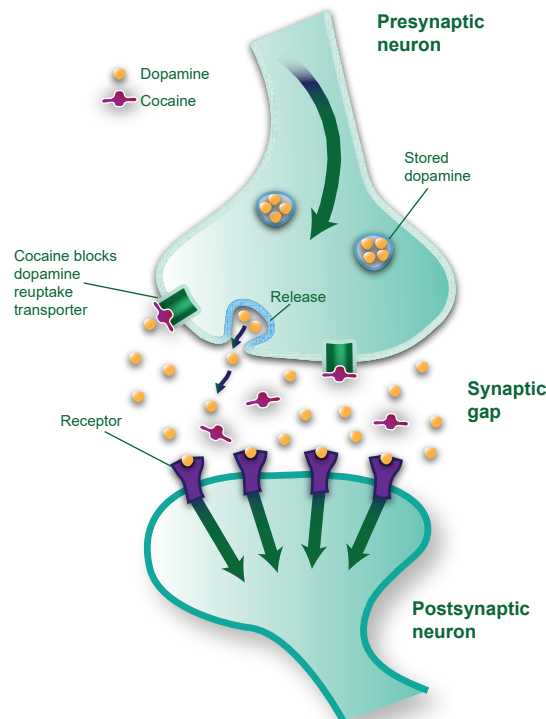
fatigue (Ciccarone, 2011). In some cases, tremors, dizziness, and muscle twitching can occur (NIDA, 2016a).

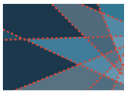
Acute Psychological Effects

The extended firing of the postsynaptic neurons resulting from prolonged dopamine receptor activity is initially experienced subjectively by people using cocaine as a positive sensation involving increased energy, arousal, and stimulation (NIDA, 2016a). The effects experienced during the initial period of cocaine use are generally mood altering in a positive manner. For most individuals, the subjective experience of the acute effects includes a generalized state of euphoria in combination with feelings of increased energy, talkativeness, mental alertness, and hypersensitivity to sight, sound, and touch (NIDA, 2016a).

Many people feel more intensely involved in their interactions with others and more playful and spontaneous when using cocaine. As patients use more, they may experience unpleasant adverse

EXHIBIT 2.4. Acute Effects of Cocaine on Dopamine Transmission





effects including increased anxiety, irritability, paranoia, and restlessness (NIDA, 2016a). As cocaine use subsides, particularly among patients with a stimulant use disorder, withdrawal symptoms will be present, including depressive symptoms and mood lability (Ciccarone, 2011).

With continued escalating use of cocaine, the individual becomes progressively tolerant to the positive effects and sensitized to the negative effects, which can increase the risk of unintentional overdose (NIDA, 2016a). People report that the positive effects of cocaine use are not as profound and that the rebound negative and adverse effects may increase over time, leading to a dysphoric, depressed state. This constant cycle of seeking additional positive effects and eliminating negative effects may perpetuate the cocaine use disorder. (For details on the medical aspects of acute cocaine use, see Chapter 3.)

Chronic Physiologic Effects

Initial experimental cocaine use often progresses to more steady use, requiring larger and larger doses to achieve the desired effects (NIDA, 2016a). Someone with regular cocaine use may become obsessed with the rituals of cocaine use and find that many common items or situations trigger cravings for the drug. Cocaine use disorder can develop, with overwhelming urges and cravings for cocaine, and an inability to self-limit or abstain from use.

The person addicted to cocaine will continue use despite the negative consequences. At this stage, the adverse consequences of cocaine use disorder have probably affected all aspects of the person's life.

There are no data that indicate how long it will take for any individual to begin to experience the chronic effects of cocaine use. Some individuals report an ability to use for extended periods with few signs of negative consequences. Others report a very dramatic onset of severe detrimental effects as soon as a few weeks or months after initiation of cocaine use. In general, however, similar to the effects of MA, the higher the doses and the more frequently the doses are administered, the more quickly the chronic effects of cocaine use will appear. In addition, intranasal administration (snorting) is associated with slower onset of chronic effects than is smoking cocaine (freebasing or smoking crack) or injecting it intravenously (Ciccarone, 2011).

Physically, the person with cocaine use disorder may appear thin or even emaciated. Personal hygiene and self-care may be neglected, and medical and dental needs may go unmet. Because cocaine suppresses appetite, the person fails to eat properly and may suffer from weight loss and nutritional deficiencies (Ciccarone, 2011). People with severe cocaine use disorder may ignore food, clothing, shelter, and sexual needs. Continued cocaine use can lead to erectile dysfunction and menstrual irregularities (Ciccarone, 2011), as well as anorexia, chest pain, and extreme fatigue.

Chronic Psychological Effects

Psychologically, cocaine's chronic effects oppose the often-desired initial effects. Chronic cocaine use increases paranoia and confusion (Ciccarone, 2011). The same substance that produced a mild sensation of arousal and decreased fatigue now causes insomnia and episodic depression.

Chronic use of cocaine may cause neuropsychological impairments (Quednow & Vonmoos, 2017; Spronk et al., 2013). Cocaine-induced cognitive deficits may affect multiple domains, but they appear to be reversible in patients with a mild or moderate cocaine use disorder within 1 year of cessation of use (Vonmoos et al., 2014).

The physical, psychological, and cognitive effects of chronic cocaine use reflect the underlying neurobiologic changes from cocaine's impact on the neurotransmitter dopamine. Spronk and colleagues (2013) found a strong association between the long-term use of cocaine and deficiencies in the following cognitive domains: attention, response inhibition (i.e., the ability to inhibit one's impulse to respond to a stimulus), working memory, cognitive flexibility, and psychomotor performance.

Although clinicians may easily pick up on the extensive health-compromising effects of cocaine use when examining the behavioral and psychological profile of patients entering SUD treatment, patients may need additional education to understand the correlation between their substance use and its negative health effects.

Methamphetamine

Routes of Administration

MA is typically taken orally, nasally (snorting/insufflation), intravenously, or by inhaling smoke vapors (smoking/inhalation). Less often, MA is taken vaginally, rectally, or sublingually. The half-life of a single dose of MA is about 10 hours across routes of administration (Cruickshank & Dyer, 2009).

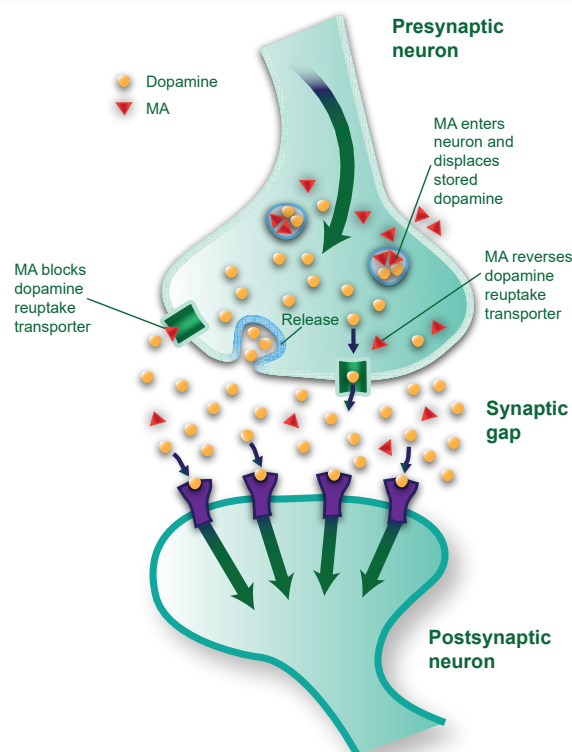
Pharmacology

The course of MA use disorder development is similar to that of cocaine use disorder. The underlying neurologic effects of MA are similar to the effects produced by cocaine: essentially, it increases levels of free dopamine in the brain's limbic reward system. (Exhibit 2.5 illustrates some of the acute effects of MA on dopamine transmission.)

Research has demonstrated that MA has neurotoxic effects, but the mechanism of action of neurotoxicity is still being studied, although it seems to be multifactorial. Oxidative stress, excitotoxicity, and neuroinflammation have all produced signals related to the neurotoxic effects of MA (Paulus & Stewart, 2020; Yang et al., 2018). Because MA crosses neuronal cell membranes and enters the microscopic sacs (called vesicles) where neurons store dopamine, it is believed that damage to the storage sacs and the neurons' axonal endings causes dopamine to leak uncontrollably into the synapse. MA can also cause neurotoxicity indirectly by moving dopamine out of the storage sacs and into the neuron's cytoplasm (i.e., the cell's internal material), where it is converted to toxic and reactive chemicals. (Exhibit 2.5 shows some of these processes.)

Exhibit 2.6 includes key terms discussed in this chapter.

EXHIBIT 2.5. Acute Effects of Methamphetamine on Dopamine Transmission



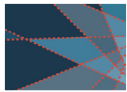


EXHIBIT 2.6. Key Terms

Excitotoxicity: A complex process in which excessive activation of excitatory amino acid receptors causes the death of nerve cells in the nervous system. Excitotoxicity can lead to the production of free radicals and oxidative stress.

Neuroinflammation: The inflammation of tissue in the nervous system resulting from a cascade of immune responses to injury or illness.

Oxidative stress: Injury to tissues in the body due to an imbalance between free radicals that cause damage and antioxidants that repair damage. Free radicals are molecules produced during metabolic reactions or after exposure to certain environmental agents.

Additionally, glutamate accumulation and microglial activity changes associated with MA use may be related to MA's neurotoxic effects. Medications that block the inflammatory effects of microglial activation may help prevent MA's neurotoxicity (Yang et al., 2018).

Numerous animal studies have demonstrated that MA can damage both dopamine and serotonin systems (Chiu & Schenk, 2012; Shin et al., 2017; Yang et al., 2018). MA toxicity occurs after repeated high-dose administration, and it is selective for certain neuronal systems, particularly those in the limbic reward system (e.g., striatum, substantia nigra, nucleus accumbens). Within these brain circuits, MA has been shown to reduce the number of nerve fibers, impair normal physiologic functioning, and destroy both axons and axon terminals (i.e., synaptic junctions). These studies have also shown that MA toxicity is highly dependent on dose, route of administration, and the frequency with which the drug is taken.

Long-term use of MA may deplete dopamine levels, decrease dopamine receptors, and lower dopamine transporter levels (Yang et al., 2018). Some postmortem studies have shown that even recreational doses of MA significantly expend dopamine levels (Boileau et al., 2016). A review on the neurotoxicity of MA (Yang et al., 2018) implicates dopamine in numerous harmful effects of MA exposure, including increased

oxidative stress (i.e., an imbalance of free radicals and antioxidants in the body), impairments in mitochondrial metabolism, and inflammatory processes within the brain.

Prolonged or heavy use of MA decreases the brain's ability to manufacture dopamine. This impairment may persist for months or even years after one stops taking MA (Yang et al., 2018). Researchers believe that those changes in dopamine levels and the damage done to dopamine and serotonin neurons are responsible for the chronic effects of MA use (Shin et al., 2017).

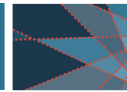
Compared with cocaine, which is rapidly metabolized by plasma and tissue enzymes, MA is metabolized at a much slower rate, which results in a longer duration of action (NIDA, 2019a). Although the half-life of cocaine is about 1 hour, a single dose of MA may produce an effect for about 10 hours (Coe et al., 2018; Cruickshank & Dyer, 2009). MA's slower rate of metabolism extends the duration of its neurotoxic effects.

Acute Physiologic Effects

The acute physiologic effects of MA are generally similar to those of cocaine: increased heart and respiratory rates, elevated blood pressure and body temperature, and pupillary dilation (Matsumoto et al., 2014). Other acute effects include increased vigor, irregular heart rate, and damage to small blood vessels in the brain (Ciccarone, 2011; Kevil et al., 2019). Dangerously elevated body temperature and severe damage to the liver occur with high-dose MA (Matsumoto et al., 2014). If not treated immediately, these effects can result in death (Matsumoto et al., 2014).

Acute Psychological Effects

MA's psychological effects, like those of cocaine, include a heightened sense of well-being or euphoria, and increased alertness (Ciccarone, 2011). High doses may produce repetitive and compulsive acts and may cause irritability; excitement; visual, auditory, or tactile hallucinations; and altered perceptions of reality, characterized by delusions and psychosis (Bramness et al., 2012; Glasner-Edwards & Mooney, 2014; Wearne & Cornish, 2018). People using MA



may engage in protective behaviors in response to irrational fears brought on by altered perceptions of reality. Mood lability secondary to elevated dopamine levels is common. With continued use, tolerance develops to the behavioral effects, and repeated exposure may produce sensitization.

MA withdrawal is like that of cocaine, but because of the longer effects of MA, withdrawal may be more intense and protracted (Courtney & Ray, 2014).

Over the course of 1 to 14 days after last use, the person using MA experiences a drastic drop in mood and energy levels. Sleep—which may be promoted by the use of secondary substances such as alcohol, barbiturates, and benzodiazepines—finally begins and may last more or less uninterrupted for several days. Upon awakening, the individual may experience mild to severe depression (Zorick et al., 2010), perhaps lasting for several weeks. While in this depressed state, the person has an increased risk of suicide (Lerner & Klein, 2019).

Chronic Physiologic Effects

Understanding the chronic physiologic effects of MA use is essential for treatment providers who serve this population. Chronic use of MA may result in multiple dysfunctions of the heart (e.g., hypertension, aortic dissection, acute coronary syndromes, pulmonary hypertension, cardiomyopathy [Kevil et al., 2019; Paratz et al., 2016; Paulus & Stewart, 2020; Petit et al., 2012]) and, among people who inject the drug, skin abscesses (Yasaei & Saadabadi, 2021) and damaged blood vessels at the injection site. Chronic use may also lead to episodes of protective behaviors, paranoia, anxiety, confusion, and insomnia (Glasner-Edwards & Mooney, 2014). Heavy use is linked to progressive social and occupational deterioration. Psychotic symptoms may sometimes persist for months or years after use has ceased (Wearne & Cornish, 2018).

Some of the most concerning research findings about MA suggest that its prolonged use not only modifies behaviors, but changes the brain in fundamental and long-lasting ways. MA impairs the functioning of both the dopamine system and the serotonin system (serotonin is another important CNS neurotransmitter; Thomas et al., 2010) and

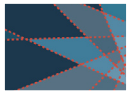
possibly other neurotransmitter systems (Ferrucci et al., 2019). MA-induced neuronal toxicity is specific to certain brain regions (primarily the limbic reward system), and this toxicity is reflected both biochemically and anatomically. Finally, these impairments in brain functioning may underlie the cognitive and emotional deficits seen in many people who use MA.

Chronic Psychological Effects

One of the potential negative effects of chronic MA use is psychosis. Patients with persistent psychosis are often treated with medications to return their brain functions to normal, and many antipsychotic medications work by affecting the activity of the dopamine and serotonin neurons. Current protocol in treating persistent MA psychosis is to manage the patient's symptoms—potentially through second-generation antipsychotics like olanzapine and risperidone—to try and improve overall quality of life and reduce the risk for recurrent use (Wearne & Cornish, 2018).

Characteristics of neurocognitive decline in people with MA use disorder are similar to those seen in patients with a cocaine use disorder. The changes to cognition are usually across multiple domains, including attention, psychomotor activity, memory, and decision making (Hart et al., 2012). Unlike with cocaine, the duration of the neurocognitive deficiencies has not been well described, but neuroimaging would suggest more long-lasting neurocognitive deficiencies likely related to the longer duration of action of MA itself and its more profound effect on the neuroplasticity of the brain.

Depletion of dopamine in the brains of people who use MA is similar to the loss of dopamine seen in patients with Parkinson's disease. Research has yet to define a clear correlation between MA use disorder and the Parkinson-like symptoms described by clinicians and patients (Christine et al., 2010; Granado et al., 2013; Kish et al., 2017). Determining the lasting effects of prolonged exposure to MA on the dopamine reward system may help clinicians better support patients entering recovery from MA use. Additionally, understanding how these Parkinsonian symptoms develop may reveal additional pathways for treatment of the condition and MA use disorder.



Prescription Stimulant Medications

Routes of Administration

Prescription stimulants are typically taken orally but, when misused, can also be taken intranasally (snorted; Yanofski, 2011). Half-lives vary by drug and by formulation (e.g., short acting versus long acting). For example, short-acting amphetamine has a half-life of approximately 9 hours, whereas the long-acting formulation has a half-life in the range of 10 to 13 hours (Pradeep & Standeven, 2019).

Pharmacology

Stimulant medications (e.g., *d*-amphetamine, mixed enantiomers/mixed salts amphetamine, lisdexamfetamine) exert their effect in much the same way that cocaine and MA do—by increasing levels of dopamine in the brain (NIDA, 2014). The prescription stimulants methylphenidate and *d*-amphetamine increase dopamine signaling—methylphenidate by blocking dopamine transporters and *d*-amphetamine by enhancing dopamine release from nerve terminals (Lakhan & Kirchgessner, 2012). Prescription stimulants are prescribed in such a way that, when taken appropriately, they produce slow and steady increases in dopamine (NIDA, 2014).

Acute Physiologic Effects

Acute adverse physiologic effects of stimulant medications include loss of appetite, insomnia, weight loss, headache, nausea, vomiting, abdominal cramps, increased blood pressure and heart rate, and, potentially, worsening of motor tics (Craig et al., 2015; Heal et al., 2013).

Chronic Physiologic Effects

Ongoing exposure to stimulants—such as repeatedly taking even the same doses of stimulant medication—can lead to tolerance to the stimulant, as well as tolerance to the brain's endogenous dopamine (Yanofski, 2011). This tolerance to dopamine means the brain becomes less sensitive to it; thus, it could become less sensitive to the medication's effects over time (Yanofski, 2011).

Other long-term effects of stimulant medication in children and adults are unclear, in part because of the lack of longitudinal treatment studies and poor long-term adherence to treatment (Molina & Swanson, 2020). For instance, it is unknown whether brain changes that occur with acute stimulant medication exposure (e.g., increased activation of areas of the prefrontal cortex that are normally underactive in ADHD) persist with chronic exposure (Molina & Swanson, 2020; Weyandt et al., 2013). There seems to be no link between prescription stimulants taken in adolescence and later development of SUDs (Quinn et al., 2017; Wilens et al., 2011). Appetite loss, headache, and digestive distress appear to continue with chronic use, but, again, few studies of long-term effects exist (Craig et al., 2015).

Acute Psychological Effects

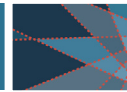
Prescription stimulants are known to improve alertness, attention, and energy (NIDA, 2018b). Thus, much of the research on the short-term effects of these medications concerns cognitive functioning, including enhancement of several cognitive processes, such as attention, vigilance, response inhibition, memory, and working memory (D. M. Dougherty et al., 2016; Molina & Swanson, 2020; Swanson et al., 2011). People misusing prescription stimulants often do so because of the perceived neurocognitive benefit—largely that of improved concentration and alertness, such as for studying and academic performance (Clemow & Walker, 2014; Marraccini et al., 2016; Weyandt et al., 2013)—and not necessarily solely as a result of craving.

Chronic Psychological Effects

Research suggests that long-term use results in continued alleviation of ADHD symptoms, including inattention, hyperactivity, and impulsivity, but only while the medication is being taken (Craig et al., 2015).

Assessment and Diagnosis

Diagnosis can be based on criteria established in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association [APA], 2013) for a stimulant use disorder

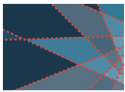


involving amphetamine or cocaine. For treatment reimbursement, the diagnosis may also need to reflect criteria according to the most recent version of the *International Classification of Diseases, Clinical Modification* (ICD–CM) found under “Coding” at <https://www.cms.gov/Medicare/Medicare> (the current version at the time of this Treatment Improvement

Protocol [TIP] update’s publication was ICD-10-CM). Arriving at a diagnosis is simplified by having information available from a relevant and accurate patient history, a urine toxicology screen or similar laboratory tests, and clinical observations of physical signs and mental status.

WHAT TO DO IF A PATIENT SCREENS POSITIVE FOR STIMULANT USE

- Primary care providers are on the front lines of identifying and helping manage SUDs in patients. Regular screening can help hasten diagnosis and referral for treatment. But once a patient screens positive for stimulant use, what should primary care physicians do? Best practices include the following (Substance Abuse and Mental Health Services Administration [SAMHSA], 2011):
- Leverage screening, brief intervention, and referral to treatment (SBIRT) techniques to get a better sense of the patient’s symptoms and severity, substance-related problems (e.g., with work, with relationships, legal problems), and treatment needs. (For more information about SBIRT, see the text box “Screening, Brief Intervention, and Referral to Treatment for SUDs: What Primary Care Providers Need to Know” in Chapter 3.)
- For mild or moderate stimulant use, a brief SBIRT intervention centered on education and motivational interviewing may be helpful in guiding patients toward acknowledging their problem behaviors and committing to behavior change. Using trained peer recovery support specialists can offer patients additional support and resources from people with lived experience with SUDs.
- For severe stimulant use, refer patients to qualified licensed mental health service providers and SUD treatment providers in the co-occurring disorders field for treatment and supportive services (e.g., for outpatient services, intensive outpatient programs, partial hospitalization services, residential programs, 12-Step programs such as Crystal Meth Anonymous).
- Use warm handoffs and other active referral linkages, rather than simply disseminating contact information, to increase the likelihood that patients will enter treatment. Providers should also have follow-up discussions with patients to ensure the referral was used. If the patient did not follow through, providers should talk with the patient to determine the reason and discuss how barriers to access can be overcome.
- Offer education about the dangers of taking stimulants laced with synthetic or nonsynthetic opioids—particularly cocaine with fentanyl, which is an increasingly popular and highly lethal combination. Educate patients and family members about the purpose of naloxone (to reverse opioid overdose) and how and when to administer it, and ensure that interested patients have a prescription for naloxone.
- For patients who inject drugs, also offer education about the importance of safer injection practices, how to obtain new needles and syringes, simple wound care techniques, and signs and symptoms of infection that warrant further medical intervention.
- For patients ambivalent about treatment, provide harm-reduction strategies and education. Providers should prescribe prevention medications like postexposure prophylaxis (nPEP) or pre-exposure prophylaxis (PrEP), screen for asymptomatic infections, provide overdose and overamping education, and create a plan for how to access treatment when the patient is ready.
- Where appropriate (e.g., when patients have a supportive family network), consider including family in the recovery process to give patients additional emotional support and resources to help with stopping stimulant use. (See SAMHSA’s TIP 39, *Substance Use Disorder Treatment and Family Therapy* [<https://store.samhsa.gov/product/treatment-improvement-protocol-tip-39-substance-use-disorder-treatment-and-family-therapy/PEP20-02-02-012>], for more guidance about the role of families in SUD treatment.)



History

An appropriate substance use history should include the substance(s) and medications used during the past 30 days; the specific substance(s) or combinations typically used with the usual dose, frequency, and route of administration; the duration of use; and the time and amount of last use (Substance Abuse and Mental Health Services Administration [SAMHSA], 2020I). If the patient has been bingeing, a brief description of this and previous episodes is helpful. In addition, the history should include information about any previous seizures, delirium tremens, heart and pulmonary problems, paranoid reactions (with or without altered perceptions of reality and hallucinations), and other serious medical and psychological conditions and psychiatric diagnoses and if they occurred pre- or post-stimulant use, as well as all medications the patient is taking. Additionally, check to see if there are substance use or psychiatric problems within the person's family (SAMHSA, 2020I).

For most patients presenting in an emergency department, the substance use and medical history will, of necessity, be brief and focus on the potential causes for the observed symptoms and complaints and any potential medical or psychological problems that are likely to complicate treatment and the patient's response. Emergency department personnel should stabilize the patient medically and assess potential danger to self and others before trying to take a history. Patients in a heightened state of arousal and experiencing persecutory perceptions may not give an accurate accounting of their current and past substance use. Information from significant others or from a reliable source can help clarify the patient's history. In situations where the patient is delirious, psychotic, or unable to respond, information from accompanying friends or significant others about the antecedents of the problem is particularly important. Sometimes, the substance use history must await symptomatic management.

The history may be supplemented by a variety of SUD screening instruments, although these are not notably reliable if used with individuals who are intoxicated or acutely psychotic.

A number of these screening instruments are described in detail in Appendix B of SAMHSA's TIP 42, *Substance Use Disorder Treatment for People With Co-Occurring Disorders* (<https://store.samhsa.gov/product/tip-42-substance-use-treatment-persons-co-occurring-disorders/PEP20-02-01-004>).

Urine Toxicology

A urine screen or toxicology test can be used to identify which substances the patient has used recently (Jaffe et al., 2016). This testing is vital to confirm clinicians' clinical assessments and observations. Some emergency departments have bedside or patient-side urine immunoassay testing kits (dipstick tests) that can be used for a quick turnaround without waiting on more formal assays. The kit's results can be validated by additional laboratory studies.

The results of either dipstick or Enzyme Multiplied Immunoassay Technique (EMIT) tests are appropriate to use for medical purposes. Alternative techniques for determining substance use are analyses of hair, blood, sweat, or tissue samples (Jaffe et al., 2016). In general, however, urine has become the standard method of determining substance use in an individual, and tests are readily available in the medical setting, whereas other types of testing are not (Jaffe et al., 2016). Urine screens are relatively inexpensive, with five-panel tests (i.e., tests for five different drugs) costing on average \$4 and 14-panel tests costing about \$7 (Jaffe et al., 2016). Both qualitative and quantitative urine assays are usually needed to verify use and time/amount taken. Repeated assays can be used to track elimination of stimulants from the system if large amounts have been detected.

Because no standard set of substances is tested in a urine substance screen, medical personnel should make certain that assays for suspected substances are included. Also, no toxicology screen can determine with certainty whether someone used any particular substance—or any substances at all. The detection limitations may be too broad or the specific substance may have been completely metabolized before a urine specimen was collected. A positive report will not necessarily indicate when the substance was last used.

Metabolites for some substances are detectable for days or weeks after last use but take some time after substance administration to be detectable in urine (K. E. Moeller et al., 2017).

MA can be detected in urine for approximately 48 hours following use, and cocaine metabolites may be detected for as long as 2 to 4 days following use (K. E. Moeller et al., 2017). Many prescription and over-the-counter medications (e.g., diet aids, cold remedies) contain phenylpropanolamine or ephedrine that may yield positive EMIT or radioimmunoassay tests for amphetamines. Certain agents (e.g., phenylpropanolamine, ephedrine) can produce cross-reactivity in amphetamine tests, causing immunoassays for the analysis of amphetamine-type substances to potentially produce false positives (K. E. Moeller et al., 2017). Urine screening tests are not confirmation of patient substance use but rather are one piece of information to help guide clinical decision making. Many substances may interact with an amphetamine screening test. For this reason, the preferred method for determination of stimulant substance use is confirmatory urine testing in the form of gas chromatography/mass spectrometry.

Physical Signs and Mental Status

Signs and symptoms of cocaine use can include extreme happiness or being very energetic; hypersensitivity to sight, sound, and touch; irritability; paranoia; and, in large amounts, bizarre and violent behavior (NIDA, 2016a). Signs of MA use can include increased attention, decreased fatigue, increased activity and wakefulness, decreased appetite, euphoric mood, (NIDA, 2019a) and, in large amounts, fever, sweating, tremors, a rapid heart rate, stroke, aggression, and paranoia (Radfar & Rawson, 2014). Increased sensitivity to noise, nervous physical activity like scratching, irritability, dizziness, confusion, extreme anorexia, convulsions, and blood pressure are also potential harmful effects of MA use (SAMHSA, 2018c). Prescription stimulant misuse can manifest as feelings of euphoria, but in large amounts can result in restlessness, tremors, overactive reflexes, rapid breathing, confusion, aggression, hallucinations, panic, high fever, muscle pains, and weakness (NIDA, 2018b).

Data acquired from monitoring vital signs (temperature, blood pressure, pulse rate, respiration rate) can be used to document physical indicators of stimulant use. In addition, observations of physical manifestations related to acute or chronic stimulant use and to withdrawal can be documented. Similarly, a variety of instruments exists to determine mental status, although observational data regarding psychological and mental status may be adequate (see Appendix B of TIP 42, *Substance Use Disorder Treatment for People With Co-Occurring Disorders* at <https://store.samhsa.gov/product/tip-42-substance-use-treatment-persons-co-occurring-disorders/PEP20-02-01-004>. [SAMHSA, 2020I]).

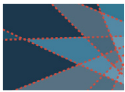
ASSESSING FOR COGNITIVE DEFICITS

Profound cerebrovascular dysfunctions can occur among people who use stimulants. Clinicians must remain vigilant for neurocognitive disorders, like delirium, as well as signs and symptoms of those disorders, like changes in memory or orientation, in patients with stimulant use because such disorders can hinder recovery. They do so by negatively affecting outcomes like abstinence and treatment retention and certain cognitive domains, like motivation and decision making (Copersino et al., 2012; Perry & Lawrence, 2017).

For indepth cognitive assessment, referral to a neuropsychologist or neuropsychiatrist may be warranted. For older adults with past or current stimulant use who are experiencing cognitive difficulties, also consider referring to a geriatrician.

Differential Diagnosis

In the diagnostic process, other disorders and conditions with similar or identical presentations must be considered. Many people with stimulant use disorder have coexisting mental illnesses such as bipolar disorder and borderline personality disorder, which share some symptoms with stimulant use disorders (SAMHSA, 2020I). A heart attack, seizure, or other type of adverse medical event that can be brought on by stimulant



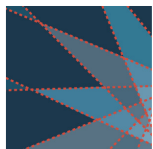
toxicity may instead have a different cause. The cause of the symptoms or adverse events must be determined for optimal continuing care and medical management.

Before a differential diagnosis of a coexisting mental disorder can be made, the patient must be abstinent for at least 4 weeks following cessation of withdrawal or severe intoxication (APA, 2013). The presenting psychiatric syndrome and symptoms can be treated meanwhile, and a diagnosis of unspecified schizophrenia spectrum and other psychotic disorders can be given. More information regarding the diagnostic process for patients with symptoms that indicate coexisting substance use and mental disorders can be found in TIP 42, *Substance Use Disorder Treatment for People With Co-Occurring Disorders* (<https://store.samhsa.gov/product/tip-42-substance-use-treatment-persons-co-occurring-disorders/PEP20-02-01-004>).

New forms of brain imaging techniques could offer a promising approach for making certain differential diagnoses—for example, if current research determines that these techniques are useful for distinguishing among drug-induced and other forms of psychosis.

Summary

Research has shown how stimulants such as cocaine, MA, and prescription stimulants exert their effects on the nervous system and affect feelings, emotional response, and behavior. There is now a greater understanding of neurologic systems related to reward and reinforcement, the development of stimulant use disorders, and the roles that craving and memory play in sustaining SUDs. Existing research can also help guide treatment approaches. Although more research is needed on the long-term neurologic, medical, psychiatric, and neurocognitive effects of stimulants in humans, animal studies have demonstrated cocaine's and MA's ability to disrupt normal brain function and cause long-lasting and perhaps permanent neurologic impairments. Continuing research and emerging imaging technologies will assist in the development of new and improved approaches for treating stimulant use disorders. Assessment of people with stimulant use should involve taking a thorough history, complemented by urine toxicology and data from physical observations. For less severe stimulant use, clinicians can use screening, brief intervention, and referral to treatment techniques to help guide patients toward behavior change. Patients with severe stimulant use disorder should be referred for specialized SUD treatment.



Chapter 3—Medical Aspects of Stimulant Use Disorders

KEY MESSAGES

- Healthcare service providers need to learn the medical signs, symptoms, and consequences of stimulant use to understand how best to medically manage patients with stimulant use disorders. Behavioral health service providers should also learn the medical aspects of stimulant use disorders so they can refer patients for medical intervention quickly and appropriately.
- The physical effects of stimulants will vary by the type of stimulant taken, route of administration, dose, purity of the substance, the individual's pattern of use, other substances the individual may be using, and any medical or psychiatric comorbidities the individual may have.
- Common medical complications of stimulant use disorders are cardiovascular conditions, respiratory problems, cerebrovascular events, muscular and renal dysfunction, gastrointestinal problems, infections including HIV/AIDS, and hepatitis C.
- Common psychological complications of stimulant use disorders include psychosis, depression, hypervigilance, and anxiety.
- People with stimulant use disorders often have co-occurring conditions that, if untreated, can exacerbate their substance use or otherwise make recovery more difficult. Co-occurring conditions of note are polysubstance use, co-occurring mental illness, medical conditions, and traumatic injury.

This chapter addresses the psychological symptoms and other medical consequences commonly seen in people using various forms of stimulants (e.g., powder cocaine, crack cocaine, methamphetamine [MA]) who appear at hospital emergency departments (EDs) and other medical settings or who need specialized medical care while participating in residential or outpatient substance use disorder (SUD) programs. The purpose of the chapter is to assist medical personnel in recognizing and treating problems in people with stimulant use that may arise secondary to acute/chronic intoxication, during withdrawal, or in various stages of recovery and in differentiating these problems from similar presentations of other medical and psychiatric conditions. The information in this chapter may also be useful to nonmedical treatment providers to help them recognize physical symptoms that would warrant medical attention and follow-up. Another emphasis is the need for establishing and ensuring linkages between medical facilities and appropriate, comprehensive SUD treatment/rehabilitation programs.

People who use psychostimulants typically present with acute medical problems such as cerebrovascular accidents (i.e., stroke), acute myocardial ischemia, heart failure, hyperthermia, or seizures. Other major symptoms manifest as altered mental status, including confusion, altered perceptions of reality (e.g., delusions), paranoid ideation, hallucinations, and suicidal ideation. Cardiovascular disease is the third leading cause of death, behind overdose and accidents, among people who use MA (Kevil et al., 2019).

Because this chapter discusses medical topics and concepts that may not be familiar to all readers, Exhibit 3.1 defines key terms that will be used.

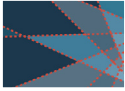


EXHIBIT 3.1. Key Terms

Altered perception of reality: A phenomenon in which the way that an individual understands or interprets external stimuli or internal sensations is distorted. The term is used in Chapter 3 specifically to refer to a **delusion**, which is a false belief based on an incorrect interpretation of reality, that is firmly believed despite evidence to the contrary, and that is not part of one's culture or religious beliefs (e.g., believing that a flickering light bulb is a sign that one is being spied on, believing that one is pregnant despite no medical indication that this is true) (Shahrokh et al., 2011). Hallucination, another altered perception of reality, is defined separately.

Alveolar rupture: A condition of the respiratory system in which pressure changes between the alveoli (air sacs) and the interstitium (a fluid filled space around the air sacs) cause a tear in the wall of the air sac that allows air to enter the interstitial space. Alveolar rupture can lead to breathing problems and lung damage.

Anticholinergic: A substance that inhibits the parasympathetic nervous system by interfering with the action of the neurotransmitter acetylcholine, which regulates neural impulses that control muscle movement. It is often used to describe the mechanism of action for a drug (e.g., anticholinergic medications).

Aortic dissection: An aortic dissection is a potentially life-threatening condition in which tears in the inner layer of the aorta, the large blood vessel that exits the heart and supplies blood to the rest of the body, lead to blood loss and separation of the layers of the aorta's wall, which can block blood flow, resulting in impaired perfusion throughout the body. Severe tears that extend all the way through to the outermost layer of the aorta are usually fatal (Mayo Clinic, 2017b).

Arrhythmia: A condition in which a person's heart rate or rhythm is abnormal due to malfunctions in electrical impulses. The heartbeat can be too fast, too slow, or irregular.

Barotrauma: An injury caused by a change in air or water pressure resulting in physical damage to body tissue, frequently affecting the ears or the lungs.

Bronchospasm: A tightening of the muscles that line a person's airway.

Bruxism: A condition in which people unconsciously or consciously grind or clench their teeth.

Catecholamine: A type of hormone that is produced by the adrenal glands or brain.

Choreoathetoid: Related to choreoathetosis, which is a movement disorder characterized by rapid or slow involuntary twitching or writhing of the body.

Conditioning: A learning process in which one stimulus signals the occurrence of a second stimulus either through pairing stimuli (classical conditioning) or applying a consequence after a behavior (operant conditioning).

Corticostriatal: Refers to the connection between the cortex and the striatum in the brain, which facilitates the flow of sensory, motor, and limbic information along a pathway to regulate motor control, action selection, and reward (W. Li & Pozzo-Miller, 2020).

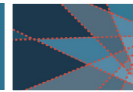
Depersonalization: A sense of experiencing one's own thoughts, feelings, and behaviors from a distance, as if observing or dreaming.

Derealization: A sense of feeling detached from one's surroundings, such that the environment appears distorted and not real.

End organ: Any organ fed by the circulatory system (e.g., heart, kidneys, brain, eyes) that can sustain temporary or permanent damage when circulation is disrupted.

Euphoria: A mental and emotional condition characterized by an intense feeling or state of pleasure, happiness, and excitement.

Continued on next page



Continued

GABA system: The network of brain receptors that respond to the inhibitory neurotransmitter gamma-aminobutyric acid.

Glomerular filtration: The process that takes place in the kidneys to filter the blood and eliminate excess fluid and waste from the body through the production of urine. The physiologic process is often expressed as a rate and used to determine the stage of kidney disease (if present).

Granulomatosis: A condition stemming from inflammatory processes that cause nodules made up of immune cells, known as granulomas, to form and affect various organs throughout the body.

Hallucination: A false sensory perception that occurs despite the fact that no sensory stimulus is present (Shahrokh et al., 2011). This could include experiences like seeing things that aren't really present (i.e., visual hallucinations), hearing voices that aren't really there (i.e., auditory hallucinations), or feeling tactile sensations that are not real (e.g., feeling like bugs are crawling under one's skin).

Hypertension: Blood pressure that is elevated above the normal range.

Hypomania: A state defined by abnormal elevations in mood, activity, or energy, typically lasting for at least 4 days. Hypomania is less extreme than mania and does not cause significant impairment in functioning.

Hyponatremia: A condition characterized by abnormally low levels of sodium in the blood, often caused by conditions such as kidney disease, liver disease, and heart failure.

Ideas of reference: The false belief that casual incidents and external events have a personal significance.

Ischemia: A condition in which blood flow to tissues and other organs is reduced, often resulting from damage to blood vessels caused by a blockage. Ischemia can occur anywhere in the body and can be classified as either partial or complete, leading to either reduction in oxygen transport or total impairment in oxygenation.

Kindling: A neurologic response, characterized by increased sensitivity to a substance, that worsens withdrawal symptoms following repeated attempts at cessation.

Metabolic acidosis: An imbalance of electrolytes that disrupts the acid-base pH balance and causes excess acid in body fluids. This condition can have severe consequences and become life threatening without medical intervention.

Myocardial infarction: Also known as a heart attack, myocardial infarction occurs when there is impaired blood flow to the heart, causing damage to the heart muscle and affecting its ability to pump blood efficiently and circulate oxygen throughout the body.

Necrosis: The premature death of cells due to external factors, such as infection or injury.

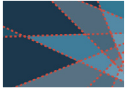
Perfusion: The movement of fluid through the circulatory system.

Perseveration: An uncontrollable persistence or repetition of a particular thought or behavior despite a clear reason for ceasing or absence of a stimulus.

Placental abruption: A sudden complication of pregnancy that occurs when the placenta partially or completely separates from the inner wall of the uterus prior to delivery, endangering the mother due to bleeding and the baby due to limited oxygen and nutrient transport (Mayo Clinic, 2020).

Pneumonitis: A condition affecting the lungs that is characterized by tissue irritation and inflammation that impairs oxygen exchange. Pneumonitis can be caused by infectious or noninfectious agents.

Continued on next page



Continued

Psychosis: A group of symptoms defined by diminished contact with reality. Individuals with psychosis can have positive symptoms characterized by odd or unusual thoughts, feelings, or behaviors, including the presence of hallucinations, altered perceptions of reality, and disorganized thoughts, speech, and behaviors. Alternatively, an individual with psychosis may experience negative symptoms defined by an absence or loss of normal behaviors and experiences, including impaired emotional responsiveness, poverty of speech, reduced motivation to complete tasks, lack of pleasure, apathy, flat affect, and social withdrawal. (See also the entries for “Altered perception of reality” and “Hallucination.”)

Rhabdomyolysis: The rapid breakdown of skeletal muscle due to injury. Rhabdomyolysis can cause permanent disability and become life threatening without medical intervention.

Sensorium: “The parts of the brain or the mind concerned with the reception and interpretation of sensory stimuli” (Merriam-Webster, n.d.-b). A clear sensorium suggests that an individual has a reasonably accurate memory and demonstrates appropriate orientation to person, place, and time.

Status epilepticus: A type of seizure with a specific duration (i.e., lasts longer than 5 minutes) or frequency (i.e., having more than one seizure within a 5-minute period, without returning to a normal level of consciousness between episodes; Johns Hopkins University, n.d.-a).

Stereotypy: Persistent, repetitive acts (e.g., body rocking, hand waving, or working through an elaborate process, such as disassembling and reassembling radios or other small gadgets) that seem to offer some relief from agitation and anxiety.

Tachycardia: An elevated resting heart rate, generally greater than 100 beats per minute for adults. In children and adolescents, the threshold for tachycardia varies with age.

Thrombotic microangiopathy: The formation of microscopic blood clots in the small blood vessels that can cause the breakdown of red blood cells, low platelet levels, and organ dysfunction, most commonly affecting the brain and the kidneys (Johns Hopkins University, n.d.-b).

Thyrotoxicosis: The presence of excessive concentrations of thyroid hormones in the body, which can increase metabolic function at the cellular level. Thyrotoxicosis is characterized by systematic alterations, including increased heart rate, sweating, anxiety, shakiness, weight loss, increased appetite, heart palpitations, heat intolerance, and difficulty relaxing (A. Sharma & Stan, 2019).

Tonic-clonic: A term used to refer to the type of seizure in which there is stiffening of the muscles (tonic) followed by rhythmic twitching or jerking of the muscles (clonic).

Urticaria: Also known as hives, urticaria is a skin reaction characterized by red, swollen, itchy bumps.

Valsalva maneuver: A breathing technique in which an individual tries to blow air (exhale as if one were inflating a balloon) while the airways are blocked (i.e., pinching the nose and closing the mouth). The technique is primarily used to restore heart rhythm when the heart is beating too fast or to diagnose a disorder of the autonomic nervous system. People who take cocaine sometimes perform this intentionally to increase the drug’s absorption and increase its effects.

Vasculature: The arrangement of blood vessels in organs within the body.

Vasoconstriction: A narrowing of blood vessels that reduces blood flow and causes increases in blood pressure.

Vasospasm: An acute or subacute contraction (spasm) of an artery that limits blood flow and reduces oxygen transport with the potential to cause ischemia and end-organ damage.

Toxicity, Addiction, and Other Adverse Reactions

Cocaine use impairs central and peripheral nervous system presynaptic nerve uptake of catecholamines, which increases catecholamine circulation (Bachi et al., 2017) and leads to impairment in the regulation of dopaminergic systems (Verma, 2015). The increased availability of extracellular dopamine as a result of cocaine exposure in the brain's reward centers is hypothesized to at least partially account for the drug's strong addiction potential and euphoric effects (Verma, 2015). This pattern is also seen in MA use, as MA both blocks dopamine reuptake and increases dopamine release (National Institute on Drug Abuse [NIDA], 2019b). Meta-analyses indicate a larger and more consistent dysregulation of dopaminergic systems with MA exposure than with cocaine (Ashok et al., 2017). The two common forms of prescription stimulants—methylphenidate and amphetamine—affect the dopamine system differently, but, like cocaine and MA, both increase extracellular dopamine. Methylphenidate primarily inhibits the reuptake of dopamine, whereas amphetamine both inhibits dopamine reuptake and also increases the amount of dopamine in the synapse (Yanofski, 2011).

The precise clinical effects of cocaine, MA, and prescription stimulants depend on a complex mixture of the pharmacologic properties and purity of the drug used; the dose, frequency of use, and route of drug administration; the person's state of intoxication or withdrawal and previous experience with the drug; the context in which the drug is used; and other concomitant medical and psychiatric factors, including simultaneous use of other substances, as well as personality attributes and expectations regarding drug reactions. All of these factors not only mediate drug effects, but also influence the person's susceptibility to an SUD and are an important part of screening and history taking (American Society of Addiction Medicine, 2015a).

Route of Administration

The method by which stimulants are taken—the route of administration—determines the dosage and the rapidity and intensity of effects. Route of administration also affects the potential for adverse reactions and the likelihood of developing an SUD. The principal routes for cocaine and MA use are oral ingestion, nasal insufflation (snorting), intravenous injection, and inhalation of smoke vapors (smoking/inhalation). These stimulants can also be taken vaginally, rectally, or sublingually. When taken as prescribed, prescription stimulants are taken orally. But when misused, they can be taken orally or by snorting, smoking, or injecting.

In general, smoking and intravenous use rapidly evoke similarly intense responses, whereas oral ingestion and intranasal administration are slower delivery mechanisms, causing lower and more gradually rising blood levels and less intense subjective responses. The fact that cocaine is seldom taken orally may be attributed to the reduced systemic bioavailability with this route of administration (Coe et al., 2018).

Smoking crack cocaine rapidly delivers a highly concentrated dose to the brain. As the efficiency of the delivery system increases, so does the intensity of both the pleasurable and the adverse effects. Subjective reports from people who smoke cocaine suggest that this route of administration delivers a more intense experience than do the intranasal or intravenous routes (Kiluk et al., 2013). Exhibit 3.2 depicts these general variations in response times according to the different routes of administration for cocaine, MA, and prescription stimulants.

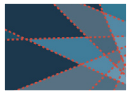


EXHIBIT 3.2. Effects of Route of Use for Cocaine, Methamphetamine, and Prescription Stimulants

ROUTE OF USE*	FORM OF DRUG	ONSET OF ACTION FOR COCAINE, MA, AND PRESCRIPTION STIMULANTS	DURATION OF SUBSTANCE EFFECTS
Oral	Powder/ pill	Approximately 30 minutes for cocaine; 15 to 20 minutes for MA; 30 to 45 minutes for both amphetamine and methylphenidate	45 to 90 minutes for cocaine; 6 to 12 hours for MA, but can continue for up to 24 hours for large doses (peak concentration 3 to 6 hours); depending on brand, 4 to 6 hours for short-acting formulations of prescription amphetamine and 8 to 14 hours for long-acting [extended-release] formulations; depending on brand, 4 hours for short-acting prescription methylphenidate and 7 to 12 hours for long-acting formulations
Intranasal	Powder	Within 3 minutes for cocaine; 3 to 5 minutes for MA	15 to 30 minutes for cocaine; 5 to 15 minutes (peak concentration) for MA
Intravenous	Solution	Within 5 to 15 minutes for cocaine and MA	10 to 20 minutes for cocaine; 4 to 6 hours for MA
Inhalation	Crystalline solid	8 to 12 seconds for crack cocaine; within minutes for MA	2 to 20 minutes for crack cocaine; up to 8 to 12 hours for MA

**Limited information is available on the pharmacokinetics of methylphenidate and amphetamine when used intranasally or intravenously or when inhaled.*

Sources: Ballester et al. (2017); Cruickshank & Dyer (2009); Drug Enforcement Administration, Diversion Control Division (2019a); Hodgkins et al. (2012); National Center for Biotechnology Information (2021); NIDA (2016a, 2019b); Reddy et al. (2020); Steingard et al. (2019).

To some extent, the dangerous consequences and addictive potential of stimulants also reflect the route of drug administration. Routes that facilitate more rapid drug delivery are more strongly linked to addiction and worse severity of addiction (Allain et al., 2015). Inhalation and intravenous injection of cocaine or MA are more strongly linked to addiction than oral, intranasal, and transdermal routes and in some cases are also linked to other harms, such as increased risk of overdose and more frequent drug use (Allain et al., 2015).

Intravenous use produces the greatest effect with the greatest risk for negative side effects compared to intranasal or oral routes. Inhalation is generally perceived as a quick form of drug delivery, producing the highest peak blood levels and the most potent subjective impact without attendant hazards from syringe needle use (Cruickshank & Dyer, 2009; Kiluk et al., 2013; National Center for Biotechnology Information [NCBI], 2021; NIDA, 2019b; Reddy et al., 2020).

Different routes of drug use also produce different side effects. People who engage in intravenous drug use can develop illnesses associated with the preparation of drugs for use (i.e., mixing/making) and the use or sharing of unsterile needles, including HIV and hepatitis B and C, loss of vein functioning (venous sclerosis) and vein scarring, the formation of blood clots within veins, and skin and soft tissue infections (Allain et al., 2015; Al-Tayyib et al., 2017; Ciccarone & Harris, 2015; Hart et al., 2014; Raiker et al., 2016). Infections introduced into the bloodstream by contaminated needles can travel via the circulatory system to any end organ, including the kidneys, brain, liver, bone, and lungs. Nasal insufflation is associated with sinusitis, loss of sense of smell, congestion, atrophy of nasal mucosa, nosebleeds, perforation or necrosis of the nasal septum, hoarseness, and problems with swallowing (Center for Integrated Healthcare, 2013; Nassar & Ouanounou, 2020). Compared with inhalation, nasal insufflation of cocaine has also been linked to longer duration of outpatient treatment, better cocaine treatment-related outcomes, and less cocaine use posttreatment (Kiluk et al., 2013).

People who use MA may recognize these route-related effects in general and may vary the routes

of administration because of specific adverse effects. For example, someone may choose to insufflate or inject MA because of irritation that it potentially causes to the lungs, or people may choose to smoke to avoid the risks associated with injection use (McCarthy & McClain, 2019).

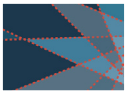
Differences Between Cocaine, Methamphetamine, and Prescription Stimulants

The major differences between cocaine, MA, and prescription stimulants pertain to the rapidity of responses and the duration of their effects (Exhibit 3.3). The sought-after effects of MA can persist for hours, whereas those from cocaine are over in minutes. Effects of prescription stimulants vary by formulation (i.e., short acting versus long acting). This has important consequences for the choice of drug and the patterns of administration adopted by individuals. The plasma concentration level refers to the amount of a drug in the plasma component of a sample of blood. Plasma concentration levels are an indicator of drug concentration (i.e., the concentration of the drug at a cell's receptor), which is important for understanding its pharmacologic effect or toxicity.

EXHIBIT 3.3. Differences Between Cocaine, Methamphetamine, and Prescription Stimulants

COCAINE	MA	PRESCRIPTION STIMULANTS
<ul style="list-style-type: none"> • Plant derived • Smoking produces a high that lasts up to 20 minutes; snorting produces a high that lasts 15 to 30 minutes • 50 percent is eliminated from the body in 1 hour • Limited medical use; used as a local anesthetic in some surgical procedures 	<ul style="list-style-type: none"> • Synthetic • Smoking produces a long-lasting high, about 8 to 12 hours • Approximately 50 percent is excreted in the urine within 12 hours • Limited medical use (e.g., attention deficit hyperactivity disorder [ADHD], narcolepsy, and weight loss) 	<ul style="list-style-type: none"> • Synthetic • Depending on brand, short-acting amphetamine produces an effect of about 4 to 6 hours and short-acting methylphenidate produces an effect of about 4 hours; depending on brand, long-acting amphetamine produces an effect of about 8 to 14 hours and long-acting methylphenidate produces an effect of about 7 to 12 hours • 50 percent of short-acting methylphenidate is eliminated in about 3 hours, and 50 percent of short-acting amphetamine is eliminated in about 7 hours; elimination of amphetamines is highly dependent on urine pH • Food and Drug Administration approved for medical use (e.g., ADHD, narcolepsy)

Sources: Courtney & Ray (2014); Hodgkins et al. (2012); NIDA (2019b, 2021b).



The plasma concentration levels of cocaine peak and decline rapidly, with a half-life of about 60 minutes (Coe et al., 2018). MA plasma concentration levels also peak rapidly but remain high for much longer, with a half-life of about 10 hours across routes of administration (Cruickshank & Dyer, 2009). Typically, the half-life of cocaine is about 60 minutes but can range from 40 to 90 minutes (ARUP Laboratories, 2019). The plasma concentration levels from smoked cocaine both peak and decline rapidly, whereas those from smoked MA also peak relatively rapidly but decline more slowly because metabolism takes longer. Regular repeated use may be more common among people who use cocaine in an attempt to sustain the drug's effects.

The half-lives and peak plasma concentrations of prescription stimulants vary by type (e.g., amphetamine and methylphenidate), brand, and formulation (e.g., short acting and long acting). Time to peak concentration for short-acting formulations of amphetamine ranges from about 2 to 3 hours; for long-acting formulations, it ranges from about 4 to 8 hours (Markowitz & Patrick, 2017). Time to peak concentration for methylphenidate is about 1 to 2 hours for short-acting formulations and about 3 to 6 hours for long-acting formulations (Mariotti et al., 2013). The misuse of long-acting methylphenidate by injecting or snorting can lead to a more rapid peak concentration level (Spiller et al., 2013).

Other factors in the preference for smokable forms of cocaine and MA include availability and price. Crack is generally less expensive and more available than powdered cocaine hydrochloride and produces, in the initial smoker, a very intense but brief rush (Drug Enforcement Administration, Diversion Control Division, 2019a). Because crystalline MA costs less per dose than other forms of MA and because the euphoria attained may persist for several hours, this form of MA delivery may be preferred. Because potential for addiction increases as time before onset of action decreases, concern about increased use of cocaine and MA pertains both to the smokable crystalline preparations and to continuing intravenous use of these drugs.

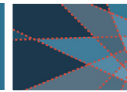
Dose

The incidence and severity of stimulant-induced side effects and overdose potential are also dose related. As the dose increases, the profile of side effects progresses from mild excitement to more intense reactions (NIDA, 2016a). Because tolerance develops rapidly to the desired euphoric effects, people using stimulants nearly always escalate dose size and frequency of drug use in pursuit of the vanishing rush. Compared with oral or intranasal routes, intravenous or inhalation use promises more rapid response rates and peak plasma concentration levels (Cruickshank & Dyer, 2009; NIDA, 2016a). People using stimulants may often change their route of use, dose, and frequency of use to achieve the desired effect (NIDA, 2019b).

Dosing patterns of MA vary by individual and pattern of use and can range broadly from 50 mg to 2,000 mg per day (Cunha-Oliveira et al., 2013). People with chronic MA use may binge in doses up to 5,000 mg per day (Cunha-Oliveira et al., 2013). Low-to-moderate doses of MA that range from 5 to 30 mg can induce arousal, euphoric mood, cardiac stimulation, and acute improvements in attention and psychomotor skills (Cruickshank & Dyer, 2009). High doses of MA (50 mg and up) can lead to psychosis (Cruickshank & Dyer, 2009).

A lethal dose of cocaine has been estimated to be around 50 mg, with documented cases of individuals having died after taking as little as 20 mg (NCBI, 2021). In low doses, cocaine can result in euphoria and agitation (NCBI, 2021). Large doses can lead to cardiovascular and respiratory dysfunctions, including hyperthermia, arrhythmias (irregular heartbeat), high blood pressure, and possibly death (NCBI, 2021; NIDA, 2016a). However, different routes of use may lead to higher concentrations in the blood, indicating a greater effect and greater potential for overdose.

Maximum doses of prescription stimulants depend on the age of the patient (i.e., child, adolescent, adult up to age 65, and older adult), the type of medication (methylphenidate or amphetamine), and the medication brand (PDR Network, n.d.). Severe tissue damage and necrosis can occur with intravascular injection, especially accidental



intra-arterial injection (Bruggisser et al., 2011). Ingestion of oral doses in mass quantities (e.g., approximately 3,000 mg) has been reported and can lead to death (Cantrell et al., 2014). Overdose of amphetamine is common and contributes to significant morbidity but is less fatal than other drugs (Spiller et al., 2013). The dosage leading to overdose depends on the patient's individual tolerance to amphetamine.

Purity of the Drug

The purity of the stimulant used also influences the rate and completeness of its absorption and effects. The purer the drug, the greater the effects. Illicit drugs, however, are seldom entirely pure. High drug purity is a public health and public policy concern that may be connected to overdose, overdose fatalities, and healthcare resource use (e.g., ED visits). In 2018, the average purity of wholesale cocaine analyzed by the Drug Enforcement Administration's (DEA) Cocaine Signature Program was 85 percent (DEA, 2019). That same year, the average purity of MA was 90 percent (DEA, 2019).

Adulterants are added to cocaine to increase its weight by cutting or substituting less expensive but similar-tasting and -acting products that will maximize profits for the seller while still satisfying the consumer. Of cocaine seized and tested by the DEA Cocaine Signature Program in 2018, 80 percent was unadulterated—an almost 36-percent increase from 2017 (DEA, 2019). Of the remainder, 17 percent was adulterated with levamisole (a veterinary drug that is not commercially available in the United States) and/or levamisole mixtures with dexamisole, and 3 percent was mixed with various other cutting agents (DEA, 2019).

A growing trend has been documented in the United States of adulterating cocaine (and to an extent MA) with fentanyl and fentanyl derivatives (e.g., acetyl fentanyl, carfentanil, furanyl fentanyl, 4-fluoroisobutyrfentanyl). From 2016 to 2017, DEA found such substances in more than 180 seized cocaine exhibits from the State of Florida. The most common adulterant of these was carfentanil, which is 10,000 times stronger than morphine (DEA, 2018). MA–fentanyl mixtures have been on

the rise since 2015 and account for 2 percent of all reports on MA from DEA and the National Forensic Laboratory Information System (DEA, 2019).

From 2013 to 2018, the number of MA-positive urine drug tests also testing positive for fentanyl increased by 798 percent, and cocaine-positive urine drug screens that also tested positive for fentanyl increased by 1,850 percent (Han et al., 2019). These combinations increase the risk of opioid overdose, as patients may not be aware that the stimulant they are taking is laced with an opioid. From January to June 2019, 32 percent of all drug overdose deaths in 24 states and the District of Columbia involved an opioid–stimulant combination, and of those combination overdose deaths, 80 percent involved illegally manufactured fentanyl (O'Donnell et al., 2020). This underscores the importance of providing people who use stimulants access to and education about naloxone (the opioid overdose reversal drug).

The manufacturing processes for illicit MA can be crude and involve many impurities and contaminants that pose serious health consequences. Until recently, most of the MA in the United States was manufactured from phenyl-2-propanone (P2P), a method of synthesis in which lead acetate is used as a chemical reagent. Production using ephedrine or pseudoephedrine as the precursor became popular in the 1990s but has decreased in popularity somewhat as access to over-the-counter pseudoephedrine has become more tightly controlled under the Combat Methamphetamine Epidemic Act of 2005. The P2P method bypasses the use of ephedrine and pseudoephedrine and yields a highly potent form of MA; consequently, P2P has become the standard production approach. More than 98 percent of MA samples analyzed in the second half of 2018 by the DEA Methamphetamine Profiling Program were manufactured via P2P (DEA, 2019).

In 2014, an alternate P2P method was identified. Termed the nitrostyrene method, it uses benzaldehyde and nitroethane as precursors (DEA, 2019). In the second half of 2018, the older P2P method accounted for 48 percent of P2P production and the newer nitrostyrene method 12 percent (DEA, 2019). DEA has identified an even more recent production method using



phenyl-acetic acid, benzyl chloride, and sodium cyanide (which form an oil called benzylnitrile), but no forensic marker currently exists, and it is unclear currently how widespread these chemical precursors are (DEA, 2019).

Illicit MA is also likely to contain potentially toxic contaminants from unintended reaction byproducts and reagent residuals, as well as processing errors. Many clandestine laboratories are operated by untrained individuals who get instructions from unpublished handwritten sources or through the Internet. As with cocaine, most of the contaminants are intentional fillers used to dilute or cut the product. Some examples of fillers are lactose, lidocaine, procaine, caffeine, quinine, and sodium bicarbonate (Cole et al., 2010). Other impurities in illicit MA can cause dangerous toxic reactions.

Patterns of Use

The effects of stimulant use also reflect the temporal pattern of drug administration and the individual's experience history or chronicity of

use. Some people use stimulants only periodically, although most discover that tolerance builds rapidly to many of the desired effects, particularly euphoria, so increasing doses and increasing frequency are needed to achieve similar effects.

Although serious medical, psychological, and social consequences have followed experimental low-dose use of stimulants, two other patterns of self-administration are of greater concern. The fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; American Psychiatric Association [APA], 2013) characterizes these as chronic or episodic, with binges occurring intermittently with brief periods of abstinence. An estimated 10 to 15 percent of people who use cocaine develop an SUD (Simon & Kreek, 2016).

Exhibit 3.4 lists the range of physiologic and behavioral symptoms often seen in stimulant intoxication (Paulus & Stewart, 2020; United Nations Office on Drugs and Crime [UNODC], 2019b).

EXHIBIT 3.4. Common Signs and Symptoms of Acute Stimulant Intoxication

PHYSIOLOGIC	PSYCHOLOGICAL/BEHAVIORAL
<ul style="list-style-type: none"> • Dilated pupils • Diaphoresis (profuse sweating)—often with chills • Hypertension • Tachycardia, with or without arrhythmia and chest pain • Decreased cardiac output • Hyperthermia (elevated temperature) • Suppressed appetite, weight loss • Nausea and vomiting • Abnormal body movements • Bruxism • Insomnia • Tremors • Headache (occasionally) 	<ul style="list-style-type: none"> • Euphoria, heightened sense of self • Increased vigor, giddiness, and sense of enhanced mental acuity and performance • Agitation, restlessness, irritability • Increased alertness • Decreased appetite • Increased sexual libido • Poor concentration, although some individuals may report improved concentration • Grandiosity, exaggerated self-esteem, egocentricity • Hypervigilance • Fearlessness • Suspiciousness, psychotic symptoms (e.g., paranoia) • Clear sensorium, not usually disoriented • Emotional lability with potential for violence, perceptions of persecution

Intoxication

The following paragraphs describe the sequence of phases that typically occur in a person as he or she moves from occasional or binge use to daily use and dependence as well as some of the accompanying side effects. Knowledge of these phases can help medical practitioners take a substance use history and understand what effects are likely to accompany a particular stage of acute intoxication, withdrawal, or more chronic use patterns.

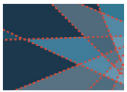
Stimulant use phases

- **Initiation, single-dose phase.** Early use of a single dose of stimulants results in euphoria and increased energy that correspond closely to stimulant plasma concentration levels. Higher levels of euphoria are achieved by inhalation (smoking) or injection routes of administration that evoke a rapid rise to peak drug concentrations. The rush experienced by people who inhale or inject stimulants is profoundly rewarding and reinforcing. Classical conditioning to the cues associated with drug use may occur during this initial phase.
- **Consolidation, dose-frequency escalation phase.** As tolerance develops to the euphoric effects, people tend to increase doses and frequency of stimulant administration in an attempt to recapture the original and most intense sensations. They may also switch the route of use to get a more rapid response. During this phase, intermittent consumption is prolonged with the discovery that higher doses produce greater effects and more frequent doses prolong those effects.
- **Maintenance phase with bingeing.** High-dose and high frequent-use patterns often lead to even more compulsive bingeing over a few hours to days that ceases only when the individual is totally exhausted or the stimulant supply runs out. Binges typically last 12 to 18 hours (but may last 2 to 3 days or longer) for people who use cocaine and much longer—from 3 to 15 days—for people who use MA. The high and sustained plasma concentration levels achieved during binges can have considerable pathological effects. The binge is characterized by frequent mood swings as plasma

concentration levels of the stimulant fluctuate. Stereotypic behaviors and thinking exclude other concerns so that the person focuses exclusively on internal sensations and withdraws from social activities in pursuit of direct pharmacologic effects. Almost all activity is directed to acquiring the drug and consuming it. Also, the settings in which the person consumes drugs become progressively restricted.

“Crash” and withdrawal syndrome phases

- **Acute withdrawal or “the crash” phase.** The timing of withdrawal phases will vary based on the type of stimulant used. Cocaine withdrawal will be shorter in duration than MA (Lerner & Klein, 2019). Withdrawal from MA use can be protracted, lasting several weeks (Courtney & Ray, 2014). Withdrawal syndromes should be thought of as a direct effect of a withdrawal from excessive dopaminergic activity throughout the body. A binge terminates with acute withdrawal, often called a “crash” (Lerner & Klein, 2019). Acute withdrawal is characterized by dysphoria, anxiety, and agitation and can begin a short time after cessation of stimulant use (Lerner & Klein, 2019). Intense cravings during the acute withdrawal phase frequently lead to recurrent substance use (Lerner & Klein, 2019). Individuals may exhibit a repetitive cycle of bingeing, with an intervening crash, over a period of several months. Anxiety and agitation are accompanied by a period of fatigue, increasing depression, and decreased mental and physical energy. An intense desire for sleep, often accompanied by insomnia, usually replaces the drug craving. During this part of the crash, individuals may use “landing gear,” such as alcohol, benzodiazepines, cannabis, or opioids, to induce and prolong sleep. During the acute withdrawal phase, patients may continue to experience psychotic symptoms related to sleeplessness or prolonged stimulant use. Additionally, in the first 1–2 weeks of withdrawal from stimulants, some patients may experience suicidality and should be monitored appropriately (Lerner & Klein, 2019).



- **Postacute withdrawal or “the wall.”** This period is characterized by a profound hypersomnolence, fatigue, mood lability, and increased appetite. People sometimes continue to have cravings during the postacute withdrawal period and return to recurrent use or a repeat binge during this period. The period of postacute withdrawal may extend to 2 weeks or more after the patient’s last use. During the immediate period after the initiation of abstinence, after psychosis subsides, patients often report anxiety or worry about painful memories lingering from the binge, and confusion about which are real and which are imagined. These disturbing events, whether real or imagined, can be traumatizing. Criminal or abusive behaviors that occur during acute intoxication, either real or imagined, can lead to feelings of remorse or dread and can contribute to impulsive self-harm behaviors.
- **Protracted withdrawal.** Following acute withdrawal, the person may experience symptoms that are opposite to those of stimulant intoxication: fatigue, loss of physical and mental energy, depression, anhedonia, and a limited interest in his or her surroundings (Lerner & Klein, 2019). Severity and duration of protracted withdrawal symptoms is often correlated with the duration and severity of stimulant use. As in previous phases of withdrawal, a severe and persisting depression in this phase can result in suicidal ideation or suicide attempts and is a major concern. Anhedonia and dysphoria can last for months in people who use MA (D. Hunt et al., 2006; Rawson, 2013). In the protracted withdrawal phase, periods of drug craving may reemerge or become stronger. These cravings are often triggered by conditioned environmental cues and can only be extinguished by sustained abstinence. Patients may also experience breakthrough psychotic episodes during the protracted withdrawal phase.
- **The post-crash euphoric phase or “the pink cloud.”** During the stage sometimes termed “the pink cloud,” patients enter a euphoric state. This often occurs around the 1-month mark following withdrawal and completion of detoxification, when the brain is overproducing dopamine. Patients may express a sense of positivity and self-confidence (“I am never

going to use drugs again!”). However, this period quickly subsides as the brain begins to underproduce dopamine, and patients typically fall into a depression at the 3- to 6-month mark, when they have a high likelihood of return to use.

Tolerance/Sensitization to Stimulant Effects

People with chronic stimulant use develop tolerance to many of the initial effects, often after only a few weeks of drug use. This means that a higher dose is required to achieve the same effects, or markedly diminished effects are attained if the same dose is continued (APA, 2013). (Note that this is not true of prescription stimulants when taken as prescribed.) Most notably, tolerance develops rapidly to the euphoric effects of stimulants and is the ostensible cause for most dose escalation by people who use stimulants, although dose increases may also stem from a desire to experience more intense effects. Tolerance also develops to the anorectic (appetite-reducing) effects of MA in humans because weight loss stops after several weeks. Tolerance also appears to develop to the cardiotoxic effects of large doses of MA that many people survive. In fact, many of the initial symptoms of stimulant intoxication disappear with chronic use: Blood pressure may be normal, and nausea and vomiting are seldom seen. This tolerance is not the result of increased MA metabolism (Cruickshank & Dyer, 2009).

Interestingly, people with chronic, high-dose stimulant use may also become sensitized to the drug, a unique phenomenon characteristic of psychomotor stimulants. Sensitization is essentially the reverse of tolerance and produces undesirable effects with lower doses of the drug than were required to yield these same reactions in an earlier phase of the addiction process. There appears to be some sensitization to the psychosis-inducing effects of stimulants in humans. After one psychotic episode is experienced following chronic, high-dose use, a lower minimal dose of cocaine or MA may induce another psychotic episode, with more rapid onset following drug intake and a longer duration than the initial psychosis. The sensitization process in stimulant use disorder is elaborated on in the “Stimulant-Induced Psychosis” section in this chapter.

Some researchers suggest that long-term use of stimulant medication may lead to tolerance in some patients and thus the need for patients with ADHD to increase their dosages over time; but it is unclear whether this tolerance and resulting need for more medication occur because of the chemical properties of the medication itself or because of other factors (Yanofski, 2011).

Clinical Manifestations and Medical Management

The intensity and duration of acute manifestations of stimulant intoxication correlate generally with the rate of rise and the height of peak blood levels reflected in brain concentrations. Acute intoxication with stimulants resembles hypomania or a manic state. In low doses, the libido (sexual drive) is stimulated; sexual desire and sexual response are enhanced (Ciccarone, 2011). Agitated states featuring increased paranoia, fear of persecution, or other psychotic symptoms may also occur with intoxication, particularly for MA (UNODC, 2019b). With increasing doses, impaired judgment, hypersexuality, and other atypical behaviors or mental alterations are more likely. Acute stimulant intoxication can result in seizures, confusion, respiratory depression, chest pain, or cardiac arrhythmias (UNODC, 2019b; see Exhibit 3.4).

Distinctive Characteristics of Methamphetamine Intoxication

- MA intoxication may be indicated by an odor of ammonia or stale urine, especially among people who smoke MA that has been crudely synthesized in illicit laboratories. Smoked MA is, however, essentially odorless.
- The person who uses MA may present with tachycardia, which may or may not be accompanied by arrhythmia (Richards & Laurin, 2020).
- People who use MA may present in the ED as a result of trauma from blunt force or penetrating injuries or from motor vehicle accidents (Richards et al., 2017).
- Given MA's longer lasting effects, its use may lead to more frequent mental impairment, more potent central nervous system (CNS) effects, and more overdoses. Chronic use of MA (beyond 2 weeks) is

more hazardous than chronic cocaine use because of MA's sustained effects. Moreover, drug-induced psychoses in people who use MA are likely to last longer than those of people who use cocaine and, in addition, may not respond as readily to available treatments.

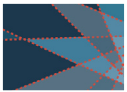
- Stereotyped activity—persistent, repetitive, and compulsive activity such as vacuuming the same part of the floor over and over again, popping knuckles repeatedly, picking at scabs, or taking apart and reassembling mechanical devices—may appear in people who use MA.
- People who chronically use MA will likely experience increased persecutory perceptions/suspiciousness (Alexander et al., 2017).
- Increased social avoidance and disorganization can occur.
- Dilated pupils and rapid eye movement can occur.

Distinctive Characteristics of Cocaine Intoxication

- People who have recently used cocaine may have increased issues with abstract concepts (as measured by problem solving in a card sorting task; Mangado & Madoz-Gúrpide, 2009).
- People who experience cardiovascular effects from cocaine are likely to return to baseline more readily than people using MA (Newton et al., 2005).

Distinctive Characteristics of Prescription Stimulant Intoxication

- Amphetamine intoxication may be less likely to produce cardiovascular problems and seizures than cocaine toxicity. Behavioral and psychiatric symptoms, such as hallucinations and psychosis, are common with amphetamine intoxication (Spiller et al., 2013).
- Rhabdomyolysis (a breakdown of muscle tissue that can release protein into the blood and damage kidneys) can occur with severe amphetamine toxicity and is often preceded by psychomotor agitation, hyperthermia, and seizures (Spiller et al., 2013).
- Distinctive signs of prescription stimulant misuse in college students can include poor psychosocial adjustment, lower academic performance (i.e., grade point average),



co-occurring use of alcohol and drugs (e.g., cannabis), and increased problems with attention (Munro et al., 2017; Rabiner, 2013).

- Behaviors indicative of prescription medication misuse in general that could appear in people with prescription stimulant misuse include stealing, forging (faking), or selling prescriptions; taking more doses than prescribed; repeatedly asking for early refills; continually claiming to have lost one's prescription (and thus needing another one); or "prescription shopping" (trying to obtain multiple prescriptions from multiple doctors; Mayo Clinic, 2018).

Management of Stimulant Intoxication

General measures to manage uncomplicated intoxication are monitoring vital signs for rising pulse rate, temperature, or blood pressure and providing a quiet and cool environment that helps to diminish agitation and overreaction to external stimuli. These measures are continued until symptoms subside, usually after several hours.

Physical exertion and an overheated room can increase the likelihood of adverse effects because stimulants affect the body's heat-regulating mechanism at the same time that blood vessel constriction conserves heat. Although verbal reassurance is usually sufficient for calming the patient, indications that agitation is escalating and moving toward paranoia and potential psychosis, with increasing risk for violence, may warrant talking with the patient about pharmacologic options (e.g., lorazepam or midazolam for severe cases in which rapid control over the patient is needed).

Background on Stimulant Overdose

Because of the rising trend of stimulants being combined with opioids, like fentanyl, risk of overdose should include the risk for both opioid overdose and stimulant overdose (Fleming et al., 2020). Variability in stimulant purity and an unpredictable and unknown relationship to body weight means overdose cannot always be predictable based on the substance used.

The symptoms of a sublethal stimulant overdose may include dizziness, tremor, irritability, confusion, mood lability, hallucinations, panic, headache, skin flushing, chest pain, palpitations, cardiac arrhythmias,

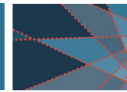
hypertension, vomiting, cramps, and excessive sweating (Richards & Laurin, 2020; Richards & Le, 2020; Vasan & Olango, 2020). High doses of stimulants may cause high fever, cardiac arrhythmias and arrest, irregular breathing, seizures, and stroke (Richards & Laurin, 2020; Richards & Le, 2020; Vasan & Olango, 2020). The development of hyperpyrexia (excessively high fever), severe hypertension, convulsions, and cardiovascular collapse signal a life-threatening situation (UNODC, 2019b). Prescription stimulant overdose is associated with pupil dilation, tremor, agitation, hyperreflexia, combativeness, confusion, hallucinations, delirium, anxiety, paranoia, movement disorders, and seizures (Spiller et al., 2013).

Lethal doses of stimulants produce a predictable sequence of events culminating in generalized convulsions and death. Heart rate, blood pressure, cardiac output, and body temperature rise rapidly, and a delirium is observed before generalized and terminal seizures begin (Mash, 2016; UNODC, 2019b). Overdose is more likely to occur when people have been abstinent for a time rather than when they have been actively and continuously using. They are at the highest risk for overdose when they enter treatment and stop using a substance.

Management of a Potentially Lethal Overdose

People who use stimulants and present with life-threatening medical conditions (e.g., arrhythmias, compromised airways, seizure) and lethal drug levels should be treated with standard life-saving techniques that respond to the presenting symptoms (NIDA, 2018b; Vasan & Olango, 2020). Acute neurologic symptoms, such as seizures or rapidly elevating vital signs, require immediate intervention. Non-drug-induced causes of any symptoms should be carefully ruled out, and the patient should also be evaluated for polysubstance use. Stimulant overdose—as well as acute intoxication and withdrawal—can be managed in hospital settings to help address medical complications and prevent symptoms from increasing in severity (UNODC, 2019b).

Management of prescription stimulant overdose should focus on providing supportive care, including the cautious use of benzodiazepines and—if



agitation, delirium, and movement disorders are unresponsive to benzodiazepines—the possible use of antipsychotics, central alpha-adrenoreceptor agonists, or propofol (Spiller et al., 2013).

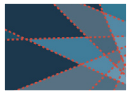
For a stimulant overdose in which opioid involvement is suspected (including fentanyl involvement), administration of the opioid reversal agent naloxone by emergency medical service personnel in the field or in the hospital setting is critical (Chou et al., 2017).

No specific antidotes or antagonists to stimulant overdose are available, unlike naloxone for opioids and the benzodiazepine antagonist flumazenil. However, the following procedures are suggested:

- Request specialist consultations as needed.
- Manage hyperthermia by rapidly cooling the patient with cooling devices or external cooling agents like water misting from convection cooling fans or ice (Richards & Le, 2020). Aggressive sedation and volume replacement may also be indicated.
- Provide adequate ventilation and oxygenation.
- Benzodiazepine therapy is generally sufficient to alleviate cardiovascular symptoms and signs. Otherwise, manage uncontrolled hypertension by administration of phentolamine. Non-dihydropyridine calcium channel blockers (e.g., diltiazem, verapamil) may be used to reduce hypertension but not tachycardia (Richards & Le, 2020). The alpha-blocker phentolamine also may be used to manage hypertension but is not effective for tachycardia (Richards & Le, 2020). Labetalol, a mixed beta/alpha blocker, has demonstrated safety and effectiveness in cocaine-induced hypertension and tachycardia (Agrawal et al., 2015; Richards & Le, 2020) and is approved by an American Heart Association/American College of Cardiology guideline for patients with unstable angina/non-ST elevation myocardial infarction who have used cocaine or MA (J. L. Anderson et al., 2007). Beta-blockers are generally discouraged in the treatment of stimulant-induced hypertension (and particularly for cocaine), although this is an unresolved matter with some guidelines offering mixed advice on their use or avoidance.
- Treat seizures like status epilepticus with intravenous lorazepam or midazolam, preferably starting first with lorazepam (H.-Y. Chen, Albertson, & Olson, 2016). If intravenous access cannot be obtained, intramuscular midazolam can be administered (H.-Y. Chen, Albertson, & Olson, 2016). Barbiturates (typically phenobarbital) are recommended only if patients do not respond to benzodiazepines (H.-Y. Chen, Albertson, & Olson, 2016).
- Complaints of chest pain warrant evaluation for possible myocardial ischemia and infarction. Nitroglycerin is indicated for cocaine-induced myocardial ischemia to alleviate coronary vasoconstriction and for cocaine-induced chest pain (Agrawal et al., 2015). Beta-adrenergic blockers such as propranolol should not be used because they may enhance vasospasm. Aspirin should be administered, unless contraindicated, to reduce cocaine-mediated prothrombotic effects (Agrawal et al., 2015).

Correction of abnormal electrolytes, dehydration, and metabolic dysfunction should lower the risk of isolated arrhythmias. If arrhythmias occur, use standard treatments. Atrial arrhythmias (e.g., atrial fibrillation, atrial flutter) that do not respond to cooling, oxygen, volume resuscitation, and sedation may require the calcium-channel blocker diltiazem as frontline parenteral (i.e., administered by injection, such as intravenous or intramuscular injection) treatment; supplemental magnesium can also be helpful (Farkas, 2021). Cardioversion is unlikely to be successful during acute intoxication. Ventricular tachycardia should be treated with sodium bicarbonate to reverse antagonism of sodium channels; if the arrhythmia is resistant to this and electrical cardioversion, lidocaine is the next choice to terminate the arrhythmia (Farkas, 2021). Also, management of acute psychiatric manifestations of cocaine intoxication by sedation appears to have a beneficial effect on emerging cardiovascular complications.

In general, phenothiazines, especially chlorpromazine, are contraindicated because they may lower the seizure threshold (M. M. Dougherty & Marraffa, 2014). Haloperidol may precipitate or exacerbate acute dystonic reactions associated with recent cocaine use (K. Lewis & O'Day, 2020).



Manifestations of Stimulant Withdrawal/Abstinence

A characteristic withdrawal syndrome usually develops within hours to days after cessation of prolonged and heavy stimulant use. The symptoms can follow long-term use or much shorter binges (Exhibit 3.5).

Some clinicians distinguish between stimulant withdrawal symptoms following a several-day binge and complaints that characterize withdrawal after more chronic high-dose use. People who use stimulants who have binged for 2 to 3 days are dysphoric and exhausted, and they sleep excessively for 24 to 48 hours. To reduce irritability and induce sleep, people may commonly use alcohol, cannabis, benzodiazepines, or opioids with cocaine or MA (often called “landing gear”). Following more chronic and regular stimulant use, severe withdrawal symptoms last several days, with less severe symptoms (e.g., fatigue, depressed mood, anxiety, drug craving, concentration difficulties) lasting 1 to 3 weeks (UNODC, 2019b).

A substantial number of people with chronic cocaine use may have subclinical evidence of withdrawal symptoms. Some people who use cocaine report withdrawal symptoms beginning 1 to 2 days after the last dose, with the crash lasting several days and withdrawal persisting from 1 to 2 weeks, with waxing and waning of the drug

craving, although protracted withdrawal may last longer (Lerner & Klein, 2019). The mood state of the person may return to normal after several days to a month.

For MA, withdrawal symptoms seem to be most severe in the initial days following cessation of use (UNODC, 2019b). There may be some physical manifestations of a withdrawal syndrome when MA use is stopped (e.g., headache, increased or pounding heart rate, sweating, muscle or joint aches; Zorick et al., 2010). Symptoms begin 2 to 4 days after a person stops use and may persist for 2 to 4 weeks (Lerner & Klein, 2019). The patient initially feels depressed and anxious, with an intense craving for MA. This phase is followed by fatigue and sleepiness, possibly mixed with insomnia. Upon awakening after prolonged sleep, the patient may be very hungry and may have persistent anhedonia and dysphoria. Other symptoms include paranoia and agitation (Lerner & Klein, 2019).

Withdrawal from MA can mimic symptoms of depression, which complicates differentiating withdrawal from an independent depressive disorder (Hellem, Lundberg, & Renshaw, 2015).

Research on withdrawal from prescription stimulants is mostly concentrated on adults and suggests that vomiting, headache/migraine, and light sensitivity can occur with abrupt discontinuation or dose reduction

EXHIBIT 3.5. Common Signs and Symptoms of Stimulant Withdrawal/Abstinence Syndrome

PHYSIOLOGIC	PSYCHOLOGICAL/BEHAVIORAL
<ul style="list-style-type: none"> • Weight gain • Dehydration • Fatigue and lassitude, with lack of mental or physical energy • Dulled sensorium • Psychomotor lethargy and retardation—may be preceded by agitation • Hunger • Chills • Insomnia followed by hypersomnia 	<ul style="list-style-type: none"> • Dysphoric mood that may deepen into clinical depression and suicidal ideation • Persistent and intense drug craving • Anxiety and irritability • Impaired memory • Anhedonia (i.e., loss of interest in pleasurable activities) • Interpersonal withdrawal • Intense and vivid drug-related dreams

(Krakowski & Ickowicz, 2018). Other withdrawal symptoms in adults include depression, fatigue, appetite change, and sleep disturbance (Krakowski & Ickowicz, 2018). Symptoms of withdrawal in children are based mostly on case studies and can include symptoms like headache, depression, and a general feeling of malaise (Krakowski & Ickowicz, 2018).

Management of Stimulant Withdrawal

No consistent physiologic disruptions requiring gradual withdrawal have been observed, but some medications may attenuate symptoms and provide support and comfort throughout withdrawal.

The greatest risk during stimulant withdrawal is of doing harm to self. Because withdrawal-related dysphoria and depression can be particularly severe in people using stimulants, risk of suicide is intensified and sensitive management is essential (Lerner & Klein, 2019). Cocaine-induced depression usually dissipates fairly rapidly—in a matter of hours to days. The depression is agitated and often related to actual situations resulting from drug use (e.g., a patient is disturbed that he has spent all his savings on the cocaine binge or that his continuing SUD jeopardizes his interpersonal relationships).

Withdrawal-associated depression/suicidality following high-dose MA use is more prolonged. During the acute phase of withdrawal, the person using high-dose MA may exhibit agitated paranoia, extreme frustration, and the return of intense drug cravings. Suicidal ideation may be high. People in MA withdrawal have been known to become violent if they perceive that they are being persecuted.

Altered perceptions of reality after acute intoxication, particularly in a binge pattern of use, may result in patients perceiving caretakers' gestures and comments as persecutory. Stress reduction techniques and other approaches to prevent harm should be used; medical personnel can also use benzodiazepines (e.g., diazepam) to control agitation and tachycardia (see the section "Aggression and Violence" in this chapter).

For patients with preexisting diagnosed or unrecognized clinical depression, stimulant withdrawal worsens symptomatology. These individuals are most likely to experience deepening dysphoria and/or paranoia after use.

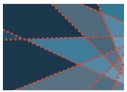
Medication management of withdrawal symptoms has not been well established in major clinical trials but might involve short-term use of sleep medications to manage insomnia or other sleep problems (Wilkerson et al., 2019). Antipsychotics are not recommended for MA withdrawal (Braunwarth et al., 2016).

Continuing agitation and persistent inability to fall asleep during the acute withdrawal stage may also be treated symptomatically by using the antidepressant trazodone, which can help to sedate the patient. Diphenhydramine is also used for its sedating properties and for its effects on the dermatologic problems that often accompany MA use (e.g., itching and hypersensitivity of the skin). However, caution should be exercised in using any medications with high potential for misuse.

During acute withdrawal, the "crash" results in patients who sleep several days at a time, depending on the dose and duration of the binge (Nishino, 2009). This hypersomnolence may interfere with assessment of mental status and physiologic functioning. Patients experiencing hypersomnolence will struggle to meaningfully engage in a treatment program and will need to be reassessed and referred during the postacute withdrawal phase, likely with additional supports.

Drug craving during stimulant withdrawal has been treated with a variety of medications (e.g., stimulant-replacement therapy [Stoops & Rush, 2013]). However, clinical evidence is limited. More research is needed in this area.

"Drug dreams" may occur during this period or as late as 6 months or more after termination of stimulant use during a protracted withdrawal phase (Jiménez-Correa et al., 2020). They usually entail vivid recall of actually using and experiencing the effects of the substance (Yee et al., 2004). The patient may actually sweat and experience other symptoms of intoxication while dreaming. These intense dreams, which may sometimes contain vignettes in which the person loses or drops a supply or refuses to smoke, can be used therapeutically to educate patients on their progress and identify potential triggers to recurrent use (Yee et al., 2004). The dreams may enhance



drug cravings and intensify a vulnerability for recurrent use. These dreams may be especially common in patients who have high ratings of drug craving and suicidality (Yee et al., 2004).

People who use stimulants will frequently self-medicate withdrawal symptoms with alcohol, benzodiazepines, or opioids. Patients may experience symptoms of withdrawal from these other substances if such use was regular or at high doses. These withdrawal symptoms require specific management and may potentially require a medication titration schedule to alleviate symptoms and prevent an acute medical event.

Withdrawal from prescription stimulants can also occur and result in fatigue, depressed mood, and sleep difficulties (NIDA, 2018b). Amphetamine withdrawal is associated with depression, fatigue, sleep problems, agitation, irritability, and concentration difficulties (Harro, 2015). There is limited research on methylphenidate withdrawal, but Food and Drug Administration (FDA)-approved labeling suggests withdrawal can include depressed mood, fatigue, vivid and unpleasant dreams, insomnia, hypersomnia, increased appetite, psychomotor retardation, or psychomotor agitation (see, for example, Novartis Pharmaceuticals, 2019).

SCREENING, BRIEF INTERVENTION, AND REFERRAL TO TREATMENT FOR SUDS: WHAT PRIMARY CARE PROVIDERS NEED TO KNOW

Screening, brief intervention, and referral to treatment (SBIRT) is a highly studied, widely used approach to ensure access to comprehensive care that has demonstrated effectiveness in identifying and treating SUDs (e.g., alcohol use disorder, tobacco use disorder) as well as depression and anxiety (Hargraves et al., 2017). Primary care providers need to be aware of SBIRT and how to implement it in their service settings, because people with stimulant use disorders and other SUDs often first present in primary care settings rather than SUD specialty treatment settings. Also, research suggests that primary care providers do not recognize and treat (or offer referral for) SUDs as often as needed (Pace & Uebelacker, 2018). Using SBIRT can help close these practice gaps.

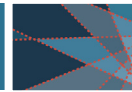
SBIRT for SUDs involves (Hargraves et al., 2017; Pace & Uebelacker, 2018):

- **Quick universal screening** (using validated measures, such as the NIDA Modified Alcohol, Smoking, and Substance Involvement Screening Test) to determine SUD presence. Quick screening often includes items to help **assess level of risk (i.e., low, moderate, or severe)** for patients who screen positive; answers to these items help determine treatment or service needs.
- **A brief motivational intervention** that educates patients about substance use and prescription stimulant misuse and helps increase their motivation for behavior change.
- **Referral to treatment and service providers** for individuals who need specialty services, a higher level of care, or both.

Best practices for primary care providers and clinics wanting to implement SBIRT for SUDs include the following (Hargraves et al., 2017; Pace & Uebelacker, 2018):

- Identify a practice champion or team lead to promote staff buy-in and increase accountability.
- Use a multidisciplinary team of professionals and nonprofessionals, such as administrative staff and information technology experts.
- Determine a screening strategy, such as which SUD screening measures will be used, who will administer them, and how the team will follow up on positive and negative screens. Nursing and intake staff can administer basic screening tools, saving time during the clinical encounter.
- Make sure the team understands the SBIRT components and their individual roles in making SBIRT a success.

Continued on next page

*Continued*

- Cultivate close relationships with referral partners and maintain lines of communication when patients are referred.
- Lay out a process for the brief intervention, such as identifying which team members will conduct the intervention and what key information needs to be conveyed to patients in the short amount of time allotted.
- Implement ongoing SBIRT training so all team members can stay up to date on policies and procedures. This includes providing staff education to reduce stigma associated with drug and alcohol addiction and to help the team understand the scientific evidence in support of SBIRT.
- Make sure SBIRT fits into the natural workflow of the office, and use visual diagrams to ensure that staff understand how and where each step of SBIRT is to take place.
- Leverage electronic health records to enhance the effectiveness of SBIRT; this will help ensure that appointments, billing, screening (e.g., reminders, flags for positive screens), and interventions are implemented, tracked, and monitored. Digital technology, such as tablets and mobile phones, can be used for screening before an appointment or while in the waiting room (Ramsey et al., 2019).
- Implement performance management tools and strategies to identify performance goals and benchmarks, barriers to implementation and positive outcomes, and potential solutions to these barriers. These efforts help organizations ensure continuous quality improvement.

Manifestations of Chronic Stimulant Use

Although fatalities from stimulant overdose or acute myocardial infarction following administration of cocaine by inexperienced people have been documented, and other medical and psychiatric complications have been observed at all dose levels and routes of administration among naïve individuals (i.e., people who previously have not been exposed to the drug), most serious stimulant-induced medical and psychological complications follow chronic, high-dose use. Potentially serious manifestations of chronic stimulant use may also be somewhat sensitive to the environment in which the person resides.

Long-term use can lead to stimulant use disorder, tolerance, and, upon cessation of use, withdrawal (UNODC, 2019b). This is also true for prescription stimulants, which are Schedule II drugs (DEA, Diversion Control Division, n.d.). A wide range of psychological and medical issues can arise with

chronic stimulant exposure, from psychosis to depressive and anxiety disorders to numerous (potentially life-threatening) cardiovascular and respiratory complications (Petit et al., 2012; UNODC, 2019b).

Although the medical consequences of chronic MA and cocaine use differ somewhat, the incidence of such side effects as chest pain, seizures, paranoid reactions, and suicidal thoughts is similar for both substances. Some studies indicate an increased risk of transient ischemic attack and sudden death/ventricular arrhythmia is associated with prescription stimulants, although more research is needed in this area (Westover & Halm, 2012). Exhibit 3.6 summarizes some of the more common symptoms and potentially serious complaints presented by chronic stimulant use or prescription stimulant misuse. Exhibit 3.7 shows the distinctive indicators of chronic MA use, cocaine use, and prescription stimulant misuse.

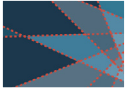
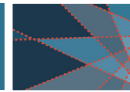


EXHIBIT 3.6. Common Symptoms of Chronic Stimulant Use or Prescription Stimulant Misuse

PHYSIOLOGIC	PSYCHOLOGICAL/ BEHAVIORAL
<ul style="list-style-type: none"> • Extreme fatigue—with physical exhaustion and disrupted sleep patterns • Nutritional disorders—extreme weight loss, anemia, anorexia, cachexia (body wasting) • Poor hygiene and self-care • Skin disorders and secondary skin infections—itching, lesions, hives, urticaria • Hair loss • Muscle pain/tenderness—may indicate rhabdomyolysis • Cardiovascular damage—from lethal doses of the drug and contaminants in MA production, with concomitant renal and hepatic problems • Hypertensive crises with renal damage from sustained hypertension • Difficulty breathing—may reflect pulmonary edema, pneumonitis, obstructive airway disease, barotrauma, and other complications • Myocarditis, infarcts • Headaches, strokes, seizures, vision loss • Choreoathetoid disorders • Impaired sexual performance and reproductive functioning • Cerebrovascular changes, including evidence of cerebral hemorrhages and atrophy with associated cognitive deficits • Ischemic bowel, gastrointestinal complaints 	<ul style="list-style-type: none"> • Paranoia with misinterpretation of environmental cues, psychosis with altered perceptions of reality, and hallucinations • Apprehension—with hopelessness and a fear of impending doom that resembles panic attacks • Depression—with suicidal thinking and behavior • Acute anxiety • Eating disorders • Mental exhaustion

EXHIBIT 3.7. Distinctive Indicators of Chronic Use of Cocaine and Methamphetamine, and Chronic Misuse of Prescription Stimulants

COCAINE	MA	PRESCRIPTION STIMULANTS
<ul style="list-style-type: none"> • Possible physical dependence and tolerance • Nasal perforations and nose bleeds among people who snort cocaine 	<ul style="list-style-type: none"> • Possible physical dependence and tolerance • In adults, increased risk of transient ischemic attack and sudden death due to ventricular arrhythmia • Dental problems, including missing teeth, bleeding and infected gums, cavities • Muscle cramping related to dehydration, with low magnesium and potassium levels • Dermatitis around the mouth from smoking hydrochloride salt • Stale urine smell due to ammonia constituents used in manufacturing MA • Various dermatologic conditions, including excoriated skin lesions 	<ul style="list-style-type: none"> • Possible physical dependence and tolerance • In adults, increased risk of transient ischemic attack and sudden death due to ventricular arrhythmia • Behaviors indicative of prescription drug misuse in general, like stealing, forging (faking), or selling prescriptions; taking more doses than prescribed; repeatedly asking for early refills; continually claiming to have lost one's prescription (and thus needing another one); or trying to obtain multiple prescriptions from multiple doctors (sometimes called "doctor shopping" or "prescription shopping")



Research on methylphenidate-specific misuse is lacking. However, knowing the signs of prescription stimulant misuse in general may be helpful in identifying long-term misuse in patients. Such signs and symptoms can include anxiety, loss of appetite, confusion, depression, irritability, memory problems, psychotic symptoms, and, in students, worsening academic performance (Greydanus, 2006). Additionally, behaviors consistent with prescription drug misuse in general could appear

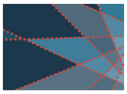
in people with chronic prescription stimulant misuse. These include stealing, forging (faking), or selling prescriptions; taking more doses than prescribed; repeatedly asking for early refills; continually claiming to have lost one's prescription (thus needing another one); or trying to obtain multiple prescriptions from multiple doctors (also sometimes called "doctor shopping" or "prescription shopping"; Mayo Clinic, 2018).

ROLE OF SOCIAL DETERMINANTS OF HEALTH IN MEDICAL COMPLICATIONS OF STIMULANT USE DISORDERS

Nonmedical influencers of health and well-being—termed "social determinants of health" (SDoH)—can play a role in the formation or exacerbation of medical conditions in people with stimulant use disorders. Common SDoH include income, housing status, employment status, education level, and adverse childhood events (like experiencing abuse or poverty as a child).

For instance, a person with cocaine use disorder who does not have access to stable housing and hygienic food preparation may be more vulnerable to contracting hepatitis A virus. Someone with MA use disorder with no job or health insurance who has developed a cardiac arrhythmia may not be able to afford (and thus adhere to) antiarrhythmic medication, which could lead to poorly controlled cardiac symptoms. When assessing patients with stimulant use disorders for possible medical conditions, clinicians should be sure to also assess for the presence of adverse SDoH. Where possible, link patients to professionals and resources that can help them address these challenges, such as mental health service providers, social workers, vocational rehabilitation services, child and family services, and financial assistance programs.

For more information, see the Chapter 6 text box "The Importance of Thinking About Social Determinants of Health" and visit the Centers for Disease Control and Prevention website Social Determinants of Health: Know What Affects Health (<https://www.cdc.gov/socialdeterminants/index.htm>).



Identification and Management of Medical Complications

The following sections briefly describe signs and symptoms of and treatments for common medical complications of stimulant use and prescription stimulant misuse. Certain populations of people with stimulant use disorders may be more likely than others to exhibit some of the medical complications described below (e.g., pregnant women exhibiting issues related to reproduction, pregnancy, childbirth, and the health of the fetus/newborn). Readers are encouraged to reference Chapter 6 for more detailed information about these special populations (i.e., people who engage in intravenous drug use, men who have sex with men, members of the transgender and gender nonconforming community, people in opioid treatment programs, individuals with co-occurring mental illness, people with medical illnesses [e.g., HIV, tuberculosis], people involved with the criminal justice system, racial/ethnic minorities, rural populations, women [including those who are pregnant], adolescents, and people experiencing homelessness/unstable housing) and consider their possible medical complications or other medical effects when developing patient-centered case conceptualizations and treatment plans.

Cardiovascular Effects

Cardiovascular complications are a leading cause of death among people who use MA. Hypertension, aortic dissection, acute coronary syndromes, pulmonary hypertension, and cardiomyopathy (heart muscle dysfunction) are frequently observed (Paratz et al., 2016; Paulus & Stewart, 2020). MA use damages the cardiovascular system via multiple mechanisms, including triggering surges in catecholamine (e.g., dopamine, norepinephrine) release, which cause vasoconstriction; direct toxicity to cardiac and vascular tissue; and inflammation of tissue and vessels (Kevil et al., 2019; Paratz et al., 2016). Hypertension and tachycardia are common and largely attributable to acute catecholamine release (Richards & Laurin, 2020). Vasoconstriction also triggered by catecholamine release can cause acute coronary syndromes and stroke. Damage to cardiac and vascular tissue, such as the endothelial

cells, by molecular mechanisms triggered by MA causes aortic dissection, dilated cardiomyopathy, arrhythmia, and pulmonary hypertension (Kevil et al., 2019). Inflammation triggered by MA contributes to functional and structural changes in the cardiovascular system, such as fibrosis and atherosclerotic plaque formation (Kevil et al., 2019; Paulus & Stewart, 2020).

Cocaine has been linked with many forms of heart disease, including different forms of arrhythmias, hypertension, coronary vasospasm, arteriosclerosis, myocardial infarction, hypertrophic cardiomyopathy, and sudden cardiac death (Kim & Park, 2019). Arteriosclerosis is seen in younger-age individuals who take cocaine, as well as in individuals with co-occurring cardiovascular risk factors (Kim & Park, 2019). Myocardial infarction can occur with both low-dose and high-dose cocaine use (Kim & Park, 2019). Studies on the association between cocaine use and cardiovascular mortality have produced conflicting results (Kim & Park, 2019). This may be due to variations in populations, as well as to study design issues, such as how studies control for other risk factors known to affect cardiovascular mortality, like cigarette smoking and depression. Some research suggests that individual factors may play a strong role in whether a person using cocaine experiences cardiovascular consequences (Kim & Park, 2019).

Life-threatening acute conditions like myocardial infarction and aortic dissection require emergency response to stabilize the patient. Treatment for these and other cardiac conditions, such as heart failure and stroke, should follow consensus-based guidelines from experts in cardiology (Havakuk et al., 2017). Sedation through benzodiazepines is a recommended treatment for cardiotoxicity and agitation (Richards & Le, 2020).

Prescription stimulants have been associated with increased resting heart rate and blood pressure (Torres-Acosta, 2020). In children and adolescents specifically, prescription amphetamine has been linked to increased diastolic and systolic blood pressure and heart rate, whereas methylphenidate in this population has been linked to increased systolic blood pressure (Hennissen et al., 2017). In some cases, prescription stimulants have

also been associated with cardiac arrhythmias, cardiomyopathy, and sudden death (Torres-Acosta, 2020). Adults with long-term use of prescription stimulants have increased risk of transient ischemic attack and sudden death due to ventricular arrhythmia, but children or adolescents with chronic use have not been observed to have increased risk (Westover & Halm, 2012).

Pulmonary Effects

Shortness of breath and chest pain can be either cardiac or pulmonary in origin. Wheezing, coughing, dark or discolored sputum, and hemoptysis (coughing up blood) can be symptoms of acute or chronic lung injury due to cocaine or MA use (Akwe, 2017; McCarthy & McClaine, 2019).

Barotrauma is a complication of cocaine use and also occurs with MA (Guck & Munyon, 2018; Restrepo et al., 2007). Barotrauma is caused by spasmodic or violent coughing following smoke inhalation, or increased airway pressure due to mouth-to-mouth drug delivery or Valsalva maneuver (Akwe, 2017; Kloss et al., 2010). Barotrauma can cause alveolar rupture and the release of air into the chest cavity, the area surrounding the heart, and even the subcutaneous tissues of the chest wall and neck. The amount of free air is usually small and resolves spontaneously under observation. Alveoli can be damaged without associated rupture and air leak. Alveoli can lose structural integrity, resulting in emphysema. Blood vessels can also be damaged causing affected patients to cough up blood and experience bleeding into the lungs (Akwe, 2017; Mégarbane & Chevillard, 2013).

The alveoli, blood vessels, and other lung tissue can be damaged in other ways as well. Mechanisms of injury to the lungs due to stimulant use include the introduction of foreign bodies or contaminants, triggering allergic or other inflammatory immune responses. Pulmonary granulomatosis, excessive bronchial reactivity or bronchospasm, and hypersensitivity pneumonitis are all possible manifestations of these types of lung injury (Akwe, 2017; Mégarbane & Chevillard, 2013). People with asthma are more likely to experience bronchospasm with stimulant use (Akwe, 2017).

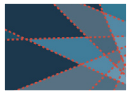
Bronchiolitis and pneumonia are common complications of cocaine use (Akwe, 2017; Restrepo et al., 2007). People who smoke cocaine can experience acute alveolitis (also known as “crack lung”), which presents with severe chest pain, difficulty breathing, and high fever but normal-appearing lung X-rays. Alveolitis requires supportive care and, in some cases, high-dose steroids. Recovery typically takes 2 weeks, but the patient may experience long-term respiratory effects (Mégarbane & Chevillard, 2013).

MA has been classified as a “likely” risk factor for pulmonary arterial hypertension—a potentially fatal condition—with the amphetamine derivatives fenfluramine and benfluorex classified as “definite” risk factors (Ramirez et al., 2018a). However, only certain subsets of people who use MA appear to develop the disease, raising questions about whether individual genetic factors confer additional risk (Ramirez et al., 2018a). One study of California hospital discharges from 2005 to 2011 showed an association with MA and both pneumonia and acute respiratory failure (H. Tsai et al., 2019). Use of amphetamine-containing diet pills has resulted in pulmonary arterial hypertension (Garg et al., 2017).

Research on amphetamine derivatives in prescription stimulants and their association with pulmonary arterial hypertension is not readily available, although at least one case report of methylphenidate-related pulmonary arterial hypertension (which subsided after treatment was ended) has been published (Ramirez et al., 2018b).

Cerebrovascular Effects

Medical consequences of stimulant use are produced in the cerebrovascular system through vascular, neuroexcitatory, and neurotoxic mechanisms. Neurologic effects of cocaine use are wide ranging and include seizures, cerebral ischemia, cerebral hemorrhages, infarction, cerebral atrophy, cognitive impairment, and mood and movement disorders (Cunha-Oliveira et al., 2014). Systemic hypertension can trigger stroke and hemorrhage within the brain tissue or between the brain and the protective layers around it. Two of the most catastrophic acute consequences of unhealthy stimulant use are damage to the blood vessels in the brain and vasospasm. MA



use has been linked to increased occurrence of hemorrhagic stroke in people younger than age 45 (Lappin et al., 2017). Damage to the heart can cause inadequate perfusion of the brain, resulting in hypoxic brain injury and subsequent edema, which can also cause lasting impairment after resolution of the acute injury (Ciccarone, 2011). Headache associated with cocaine use is also triggered by vasoconstriction or inflammation of cerebral vasculature (Farooque et al., 2020).

Seizures are a well-known complication of stimulant use (Klega & Keehbauch, 2018) triggered by neuroexcitation. Seizures triggered by cocaine tend to be short tonic-clonic events that stop without intervention and have no residual effects, but repeat seizures are typically managed with intravenous benzodiazepines. Seizures that don't stop on their own should be managed according to standard protocols for status epilepticus. Focal seizures should trigger an evaluation for stroke or hemorrhage (Zimmerman, 2012).

Neuroexcitation can also cause movement disorders and dystonia (Asser & Taba, 2015). Movement disorders consist of repetitive behaviors. Dystonia is the involuntary contraction of muscles in the face, neck, limbs, or other body parts. Dystonia can be painful and distressing (Ciccarone, 2011). Symptoms of these disorders typically resolve within a few days of discontinuation of stimulant use, but movement disorders or psychomotor disturbances, like tics and problems with gait and fine motor skills, have been seen in people who use MA and may persist even after a year or more of abstinence (Lappin et al., 2018). Benzodiazepines or neuroleptics may be used to manage acute, distressing, or persistent symptoms that impair function (Asser & Taba, 2015). More data are needed regarding the long-term management of patients with persistent movement disorders secondary to stimulant use.

Evidence from a small number of animal and human studies suggests that MA use may moderately increase the risk of developing Parkinson's disease or parkinsonism, including possibly causing premature onset of Parkinson's disease—especially when other risk factors are present (e.g., comorbid HIV infection, male gender;

Lappin et al., 2018). The potential increased risk of Parkinson's disease specifically has not been observed among people taking cocaine (Lappin et al., 2018).

Acquired brain injury is another mechanism contributing to the cerebrovascular consequences of stimulant use. Cocaine induces lesions and atrophy, mostly in the prefrontal cortex and basal ganglia (Cunha-Oliveira et al., 2014). MA is known to induce damage to dopamine and serotonin axon terminals in the striatum, prefrontal cortex, and hippocampus (Halpin et al., 2014). Cocaine and MA use have both been associated with deficits in executive functioning (decision making) and processing speed, often due to problems with perseveration, inattention, and working memory difficulties (Hall et al., 2018). Cocaine use has been linked to worse verbal working memory than MA, whereas MA has been associated with poorer delayed contextual verbal memory and delayed visual memory than cocaine (Hall et al., 2018). Cognitive deficits observed in cocaine and MA use are also seen in brain aging and dementia and may indicate premature brain aging, possibly due to cerebral atrophy resulting from direct effect of stimulants or hypoxic brain injury in people with stimulant use disorders.

Simultaneous alcohol and cocaine use produces cocaethylene, the ethyl ester of benzoylecgonine, and is also being researched further (A. W. Jones, 2019). (For more on the hazards of combining these two substances, see the "Polysubstance Use" section later in this chapter.) Another unresolved issue is whether stimulants are causal factors in CNS vasculitis; however, CNS vasculitis induced by MA or cocaine use is rare (Younger, 2019). People who have taken cocaine or MA and complain of sudden headache should be evaluated for possible intracranial hemorrhage (Farooque et al., 2020).

Case reports of current or past history of cocaine use have found an association with corneal or retinal nerve damage (Friedman et al., 2010; Stuard et al., 2017), and in some instances the damage may be similar to optic nerve damage found in people with diabetes (Stuard et al., 2017).

Although amphetamine-type substances have been hypothesized to increase the risk of stroke, a literature review of stroke incidence associated with prescription stimulant use found very little research on the subject and noted the need for additional, more robust research (Indave et al., 2018). Additionally, some studies have indicated long-term use of prescription stimulants might increase the risk of transient ischemic attack, but, again, more research is needed to reach firm conclusions (Westover & Halm, 2012).

People with ADHD are at an increased risk for seizures, but current evidence strongly suggests this is not due to stimulant medication (Wiggs et al., 2018). In an analysis of more than 800,000 insurance claims, ADHD medication use was associated with lower odds of seizure (Wiggs et al., 2018).

Muscular and Renal Toxicity

Cocaine and MA may directly cause muscle degradation, and acute rhabdomyolysis has been diagnosed in people who did not have any of the previously associated risk factors (i.e., hyperthermia, agitation, seizures, hypotension, toxic delirium or coma, acute renal failure [A.D.A.M. Medical Encyclopedia, 2021; Lannett, 2020]). Muscle necrosis may occur regardless of the route of drug administration, and the presence of rhabdomyolysis should be considered in patients with stimulant intoxication, particularly those presenting with myalgia, lower back pain, or muscle tenderness.

Cocaine is known to induce acute kidney injury, possibly through rhabdomyolysis, vasculitis, infarction, thrombotic microangiopathy, or severe hypertension (Goel et al., 2014; Pendergraft et al., 2014; Zimmerman, 2012). In the Healthy Aging in Neighborhoods of Diversity across the Life Span study (Novick et al., 2016), lifetime cocaine use was significantly associated with reduced renal functioning as measured by albumin-to-creatinine ratio (odds ratio = 1.8) and estimated glomerular filtration rate (odds ratio = 1.4). MA is associated with acute kidney injury, hyponatremia, and nontraumatic rhabdomyolysis (Pendergraft et al., 2014). Patients with stimulant use disorders should be encouraged to hydrate and take rest periods to minimize the risk of the development of renal toxicity/rhabdomyolysis.

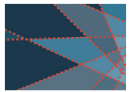
Gastrointestinal Effects

Some people who use stimulants experience abdominal pain, nausea, and vomiting, potentially indicating intestinal ischemia caused by vasospasm in the intestinal blood supply. Intestinal ischemia can lead to death of bowel tissue. Severe bowel infarction due to stimulant use has been reported (J. E. Anderson, Brown, et al., 2018; Attaran, 2017; Choi et al., 2019). Severe bowel infarction causes bleeding, elevated white blood cell counts, and metabolic acidosis, and can lead to shock and death. Even in the absence of infarction, intestinal ischemia associated with cocaine use may carry a higher risk of death compared with intestinal ischemia not caused by cocaine use. In one study, the prevalence of in-hospital death was 26 percent among people with cocaine-related intestinal ischemia versus 7.7 percent with non-cocaine-related intestinal ischemia (Elramah et al., 2012). Obstruction, perforation, and infarction are associated with cocaine use by any route of administration (Zimmerman, 2012). Although less common, gastrointestinal hemorrhage and pancreatitis can also occur from cocaine use (Carlin et al., 2014).

Reduced appetite is one of the most common adverse effects of prescription stimulants, with stomach ache, abdominal pain, dyspepsia, and weight loss also occurring (Cortese et al., 2015; Holmskov et al., 2017; Storebø et al., 2015).

Infections

As already noted, intravenous injection of cocaine or MA is associated with a variety of infectious diseases. Intravenous injection is not the most common method of misusing prescription stimulants, but it can and does occur. Individuals who inject prescription stimulants are at risk for the same injection-related infections as people who inject cocaine or MA. People engaging in injection drug use are at increased risk of infectious endocarditis, which accounts for 5 to 25 percent of hospitalizations for acute infection among people who inject drugs (Visconti et al., 2019). Increased HIV and hepatitis B and C transmission are likely consequences of stimulant use, particularly in individuals who inject intravenously and share equipment. HIV and other blood-borne pathogens may spread through communities of people



injecting drugs via shared injection equipment or unprotected sex. People who injected drugs accounted for 9 percent of all new cases of HIV diagnosed in 2017 (Centers for Disease Control and Prevention, 2021b). MA or cocaine use in the presence of HIV or hepatitis C virus can accelerate virus replication and impaired immunity, resulting in overall disease progression (NIDA, 2016c; Soontornniyomkij et al., 2016).

MA is also implicated in a host of infectious diseases, such as skin infections (cellulitis, skin abscesses), methicillin-resistant *Staphylococcus aureus* (MRSA), sexually transmitted infections, and opportunistic fungi (e.g., *Histoplasma capsulatum*; Salamanca et al., 2015). High-risk sexual behaviors, malnutrition, harmful effects of MA on immune system functioning, and inflammation likely contribute to infectious disease risk.

Cocaine use carries a significant increased risk of sexually transmitted infections such as syphilis, trichomoniasis, hepatitis C, HIV, and human papillomavirus and associated complications such as precancerous cervical abnormalities and pelvic inflammatory disease, and invasive pneumococcal disease. Tuberculosis, bronchitis, pneumonia, injection site infections, and MRSA infection are all also more common among people who use cocaine (Butler et al., 2017).

Improved access to treatment of HIV infection and prevention efforts can help address the elevated risk of HIV infection among people who use stimulants. Prevention of HIV infection may include screening and diagnosis of other bacterial or viral sexually transmitted infections, access to nonoccupational postexposure prophylaxis, and pre-exposure prophylaxis (PrEP; Nerlander et al., 2018; UNODC, 2019a; Workowski & Bolan, 2015). Given the multimodal risk factors for acquisition, including injection drug use and sexual transmission, the current recommendation for PrEP should be the use of tenofovir disoproxil fumarate with emtricitabine (Mayer et al., 2017). FDA also approved emtricitabine with tenofovir alafenamide for PrEP in individuals having nonvaginal sex (FDA, 2019). Multiple studies support the treatment of HIV as a prevention modality in patients using stimulants (Nerlander et al., 2018; UNODC, 2019a),

as even imperfect medication adherence may result in viral suppression and decrease the likelihood of transmission.

Reluctance to get tested for HIV and fear of being stigmatized by healthcare personnel may result in delays of HIV diagnosis (UNODC, 2019a). Patients with MA use in particular may have a lower CD4 nadir and may meet the criteria for an AIDS diagnosis within 6 months of HIV diagnosis. Frequent low-barrier testing and immediate access to antiretroviral therapy may improve overall outcomes for patients with co-occurring HIV and stimulant disorder (UNODC, 2019a).

Hypersexuality and lowered inhibitions for patients who use stimulants should warrant a comprehensive sexual health screen. Regardless of the patient's identified sexual orientation it may be prudent to offer multisite (i.e., vaginal, rectal, penile, pharyngeal) sexually transmitted infection testing to identify and treat bacterial infections early (UNODC, 2019a). Patients engaging in sexual activities with elevated risk for sexually transmitted infection should be screened for chlamydia, gonorrhea, and syphilis at least every 3 to 6 months or more frequently depending on their individual risk (Workowski & Bolan, 2015).

Harm reduction strategies related to skin and soft tissue infections should focus on the processes for injection that require sterile technique and should identify substances that may produce increased risks for infection (Saldana et al., 2020). Providing access to items to cleanse the skin prior to injection, safer injection techniques, and postinjection care are all important aspects of preventing skin and soft tissue infections (Hartnett et al., 2019; Saldana et al., 2020). Furthermore, for patients injecting crack cocaine who require an acid pairing to neutralize the base pair for injection, education should be provided regarding safer acid pairings, like ascorbic acid (British Columbia Center for Disease Control, 2011). Increased fungal infections, including endophthalmitis, have been well described in patients who have used natural acids like lemon juice to neutralize the base for injection (British Columbia Center for Disease Control, 2011).

For patients engaging in vaginal or anal consumption of stimulants, there is an elevated risk for toxicity and in some cases overdose or death (P. Jones et al., 2014). Patients using MA intravaginally or intrarectally should be educated on safety procedures to avoid tearing of rectal or vaginal tissues that may result in fissure or other microscopic tearing. Dissolution of the crystalline substrate is imperative to reduce the risk of microtears and associated acquisition of sexually transmitted infections.

Hepatotoxicity is a rare side effect of methylphenidate, but liver values should still be monitored throughout treatment (Tong et al., 2015). A review of the literature reveals few cases of methylphenidate-induced liver damage, and cases that do exist were generally mild in severity and resolved with discontinuation of methylphenidate (Tong et al., 2015).

Effects on Reproductive Function and on Fetus/Newborn

Chronic, high-dose stimulant use can affect reproductive and sexual functioning in both males and females. Men report gynecomastia (development of breasts), loss of sexual interest, impotence, and difficulty in maintaining an erection or ejaculating (Del Río et al., 2015; Longheu et al., 2016). Long-term stimulant use can lead to menstrual cycle irregularity (Shen et al., 2014). This may lead some women to believe they cannot become pregnant, which may not be true. Testing for pregnancy and regular use of birth control should be encouraged.

Cocaine effects on pregnant women include high blood pressure, heart attack, kidney failure, decreased platelets, and stroke. Pregnancy may increase the cardiovascular toxicity of cocaine, resulting in cardiac morbidity and mortality in otherwise healthy pregnant women (Smid et al., 2019). The constellation of cocaine effects—including high blood pressure, low platelets, swelling, protein in the urine, and seizure—can be mistaken for preeclampsia or eclampsia (Maagdenberg et al., 2006). Hypertension in pregnancy is often treated with labetalol or other beta blockers, but these drugs are associated with coronary vasoconstriction and end-organ ischemia when used concurrently with cocaine.

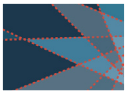
Preterm birth, low (less than 2,500 grams) birth weight, and newborns that are small for gestational age are all adverse perinatal outcomes associated with cocaine use (Gouin et al., 2011). Smoked cocaine specifically is associated with smaller head circumference (Dos Santos et al., 2018). There is a suggested association between increased risk of miscarriage, still birth, and placental abruption and cocaine use, with a somewhat more marked association between at least partial placental abruption and crack cocaine use specifically (Dos Santos et al., 2018).

There is uncertainty about the connection between cocaine use in fetal structural abnormalities, because of studies' poor control of common confounding variables such as maternal age, poverty, stress, co-occurring psychiatric conditions, and the use of other substances such as tobacco and alcohol. Concern persists about a possible link between cocaine use and defects in the genitourinary systems, limbs, and heart (Hetea et al., 2019).

Maternal cocaine use increases the risk of transmission of HIV and syphilis to the infant (J. A. Cook, 2011; Smullin et al., 2021). Problems of growth, cognition, language and motor skills, attention, affect, and neurophysiology have been described in children with prenatal exposure to cocaine (Smid et al., 2019). However, the evidence linking these findings to prenatal exposure to cocaine is less compelling than the evidence for association with gestational age; caregiver psychiatric illness; other prenatal exposures such as tobacco, cannabis, and alcohol; or the conditions of the postnatal environment.

Women who use MA are at substantially higher risk of death than those who do not (26 times higher rate of death) or men who use MA (9 times higher rate of death [Smid et al., 2019]). Reported lifetime use of MA is associated with pregnancy in adolescence (Smid et al., 2019). Pregnant women who use MA are more likely to be younger than 24 years old and are more likely to have significant psychiatric disorders (Smid et al., 2019), including ADHD (Marraccini et al., 2017).

Women who use MA during pregnancy are at higher risk of high blood pressure, heart attack, and cardiomyopathy (Smid et al., 2019). These



conditions produce more infant morbidity in pregnancies exposed to MA than in pregnancies exposed to cocaine. Cleft palate has a clear association with prenatal MA exposure, but the link with other birth defects is not yet established (Smid et al., 2019). Exposure to MA, a neurotoxin, may impact metabolism, chemical signaling such as with serotonin, and structure of the developing fetal brain (Smid et al., 2019). Gestational age and sex may be important considerations, whereas concurrent exposure to alcohol and tobacco are confounding variables (Smid et al., 2019).

MA use in pregnancy is associated with low birth weight, lower than expected gestational age at delivery, and smaller head circumference (Wright et al., 2015). Using MA throughout all trimesters has been linked to insufficient prenatal care, early delivery, and lower birth weight (Wright et al., 2015). Adverse perinatal outcomes including preterm birth, fetal growth restriction, and fetal death have been described, but studies have not been able to determine whether these outcomes are caused by MA or other factors such as contaminants, other drugs, cigarette smoking, or poverty.

At birth, infants exposed to stimulants may manifest symptoms suggestive of withdrawal. As with other newborns with substance exposure, implementation of the Eat Sleep Console model of caring for the mother and infant as a dyad, focusing on nonpharmacologic care and treatment of the newborn, has produced positive results (Dodds et al., 2019). The most common presenting symptoms are lethargy, sleepiness, and poor feeding. Stimulant-exposed infants may have difficulty being consoled (Anbalagan & Mendez, 2021); the action of consoling can increase crying because of damage to the infant's nervous system. The interaction between this and the stimulant-affected mother's low frustration tolerance (due to protracted withdrawal) can interfere with bonding and create negative feedback, psychologically and neurologically. Congenital malformations rarely occur because of stimulant exposure; those that do tend to affect the heart (Huybrechts et al., 2018). Risk of sudden infant death syndrome may be heightened slightly. Any reduction in stimulant use is correlated with improved outcomes for the baby.

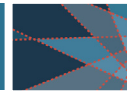
Few infants exposed to MA require intervention. For those that do, supportive feeding is often sufficient (Oei et al., 2012). A prospective study of MA-exposed mother–infant pairs matched with non-MA-exposed mother–infant pairs in New Zealand has provided valuable insights into infant and childhood development (L. M. Smith et al., 2015). Among MA-exposed pairs, this study has described increased anxiety, depression, and attention problems in children ages 3 to 5 and poorer cognitive outcomes at 7.5 years old. Imaging studies have identified sex-dependent structural brain changes, but the clinical and functional importance of these changes is not known. Of note, fetuses exposed to MA mixed with fentanyl may be at risk for opioid-related effects, such as poor fetal growth, preterm birth, stillbirth, specific birth defects, and neonatal abstinence syndrome (Centers for Disease Control and Prevention, n.d.-a).

Little is known about the impact of misuse of prescription stimulants on pregnancy, the fetus, or development. Existing knowledge is based on studies of therapeutic use of prescription stimulants. Exposure to prescription stimulants during the first trimester has not been shown to be associated with congenital defects (Andrade, 2018). Third-trimester exposure has been associated with some instances of intrauterine fetal death (Wright et al., 2015). However, a recent review of eight studies investigating the effects of ADHD medication use during pregnancy found no evidence linking this medication to negative effects on pregnant women or their children. The authors cautioned against drawing definitive conclusions given the small number of studies included in the review (L. Li, et al., 2020).

Dental Effects

Missing and filled teeth, cavities, and gum disease are all more common among people who use drugs (Yazdanian et al., 2020). Cavities are the most common dental problem among people who use drugs (Shetty et al., 2010).

People who use MA are 4 times as likely to have cavities and twice as likely to have untreated cavities compared with people who do not use drugs and have double the risk of decayed, missing, or filled teeth (Shetty et al., 2016). One



study of 552 people with MA use revealed that 96 percent had cavities, 58 percent had untreated cavities, 29 percent had severe periodontitis, almost 60 percent were missing one or more teeth, 7 percent were completely without their natural teeth, and only 23 percent still had all of their natural teeth (Shetty et al., 2015).

Fewer studies are available on the oral health of people who use cocaine, but gum disease and cavities are both positively associated with cocaine use (Bahdila et al., 2020). Cocaine is also associated with problems of the oral cavity, including oral ulcers, nasal necrosis, palate perforation, and oral candidiasis (Maloney, 2010), particularly with oral consumption and nasal insufflation (Fratto & Manzon, 2014). Oral or nasal administration of cocaine has been associated with oral lesions, receding gums, and dental erosion (Fratto & Manzon, 2014).

MA use was previously thought to have a direct chemical effect on the mouth and teeth that contributed to extensive dental disease. Comparison with National Health and Nutrition Examination Survey participants shows that elevated rates of dry mouth and regular consumption of one or more sugary beverages per day to compensate for it, along with poor dental hygiene and lack of preventive dental care over a prolonged period, underlie the problem (Clague et al., 2017). Longer history of substance use, polysubstance use, and concurrent tobacco use are all associated with worse oral health. Smoking MA was not more strongly associated with dry mouth or cavities than was snorting or injecting MA (Clague et al., 2017). Amphetamine use has been linked to broken or missing teeth, bruxism, gingival enlargement, cavities, and dry mouth (Fratto & Manzon, 2014).

People who use stimulants should receive education about preventive oral hygiene and the role of sugary drinks in the widely recognized dental problems affecting this population. Engagement, prevention, and treatment programs should provide the education and resources needed for people who use stimulants to maintain oral hygiene (Shekarchizadeh et al., 2013). Preventive dental care may be available under some Medicaid plans, at a dental school, or in a

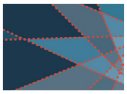
community clinic. Strategies to reduce the negative effects of dry mouth should also be considered by treatment programs. Use of hard candy or chewing gum by patients with dry mouth or bruxism may help to alleviate some of the symptoms.

A program should not make its efforts in this area contingent on someone with a stimulant use disorder deciding to enter treatment or achieving recovery. Poor dentition and oral health may also be associated with an increased risk for serious or life-threatening infections, including infective endocarditis or abscess. Prevention of periodontal disease should be viewed as a form of care for patients in active stimulant use.

Peripheral Vascular and Nerve Damage

Stimulants can damage the central nervous and cardiovascular systems regardless of the route of administration. Use of any substances by injection can be uniquely harmful to the peripheral nerves and vessels (Delaney et al., 2020; Raiker et al., 2016). Peripheral nerves control muscle use and sensation outside of the brain and spinal cord. They are fragile and can be easily damaged if struck by a needle during injection drug use. The peripheral vascular system comprises all the arteries and veins outside of the chest and abdomen. Use of any drug by injection can damage veins and arteries (Delaney et al., 2020; Raiker et al., 2016). All of the problems associated with use of drugs by injection described below are exacerbated by the chemical properties of all stimulants. Cocaine and MA cause vasoconstriction, especially near the injection site (Raiker et al., 2016). When blood flow is restricted, tissue dies, making damage to vessels and nerves as well as skin and muscle more pronounced among people who use stimulants by injection.

For patients who may use substances adulterated with levamisole, there is an elevated risk of levamisole-induced vasculitis (Abdul-Karim et al., 2013; George et al., 2019). Quick recognition of the signs and symptoms of levamisole-induced vasculitis may help in the evaluation of patients with severe presentations, including leukopenia or agranulocytosis. Most studies indicate resolution of symptoms with cessation of cocaine/levamisole consumption, but other studies have used oral steroids with unclear benefits over cessation of use alone.



The repeated puncturing of veins during injection drug use causes inflammation (phlebitis), scarring, and stiffening (Dunn & Gauthier, 2020). Injection drug use can also damage the function of veins (Delaney et al., 2020; Raiker et al., 2016). When valves in veins are damaged, blood pools in the surrounding tissues and in the venous system below the damaged area. Accumulated damage to the veins may cause venous insufficiency (Dunn & Gauthier, 2020). Venous insufficiency causes swelling of the extremities and discolored, thickening, scaling, and peeling skin. The affected extremity can be painful, hot, or itchy. The skin becomes fragile and heals poorly if at all and may result in chronic, weeping wounds. Both phlebitis and venous stasis increase the risk of formation of blood clots in the damaged veins. Clots in the arms or legs can break apart causing a thromboembolic event. If pieces of a clot travel to the lungs or heart, death may occur. A growing body of research has linked cocaine use to increased odds of developing venous insufficiency and venous thrombosis (Griffin & Cha, 2019; T. Sharma et al., 2019).

Arteries are deeper and harder to reach, but people who inject drugs may accidentally inject into arteries instead of veins (Lokoff & Maynes, 2019). Injecting into the artery is painful and can cause extensive bleeding. It also causes the drug to be delivered downstream into the extremities rather than to travel toward the lungs, heart, and brain. The extremities can become inflamed due to immune response provoked by the drug. Injection into the artery carries a high risk of clot formation (Lokoff & Maynes, 2019). The pressure in the arterial system pushes a clot until it lodges in a narrower artery; this is called a thromboembolism. Tissue past the clot no longer receives oxygen-rich arterial blood and begins to die in much the same way heart muscle dies during a heart attack. Like a heart attack, arterial blood clots are a medical emergency.

Like arteries, nerves are sometimes hit accidentally during injection drug use (Dunn & Gauthier, 2020). Hitting a nerve causes intense electric or burning pain both above and below the injection site (Dunn & Gauthier, 2020). After the injury, pain and abnormal sensations like burning or neuropathy (pins and needles) in the area served by the nerve can persist. Other forms of nerve damage also may occur with cocaine or MA use (e.g., nerve

compression; Dunn & Gauthier, 2020). In a sample of more than 900 people with injection drug use (Colledge et al., 2020), nerve damage was the most commonly reported injection-related injury and disease, occurring in 19 percent of the sample.

Injection drug use can lead to a loss of vein functioning (venous sclerosis) and vein scarring, which in turn can increase the risk of vascular disorders, like deep vein thrombosis (formation of a blood clot within the vein, which can then travel to other parts of the body, like the lungs) and skin and soft tissue infections (Ciccarone & Harris, 2015; Raiker et al., 2016). People at risk for injection drug use should have access to a sterile syringe for each use. Reusing a syringe—even one's own—increases the risk of infection. Dull or damaged needles tear and abrade delicate veins, increasing the risk for venous complications. Thorough, nonjudgmental education in phlebotomy techniques, including identifying appropriate sites for injection, rotating injection sites, and sterilizing injection equipment, should be provided. People who use injection drugs should be trained to recognize potentially life- or limb-threatening complications and apply first aid to common complications. Opportunities for wound assessment and care should be a standard part of outreach, prevention, and harm-reduction services for people who use drugs.

Identification and Management of Mental Complications

Stimulant-Induced Psychosis

Initially described by D. Young and Scoville in 1938, amphetamine-induced psychosis usually is a brief and spontaneously remitting paranoid state that is frequently accompanied by intense, fear-evoking altered perceptions of reality and hallucinations, but with clear consciousness and a relatively intact formal thought process (McKetin, 2018). Stimulant-induced psychosis occurs while the person is intoxicated, but may recur when a patient is in withdrawal or has been abstinent for many months (McKetin, 2018). The condition is not rare or idiosyncratic but typically follows chronic, high-dose use of amphetamines, MA, or cocaine and a lack of sleep. However, this drug-induced psychosis is seen more frequently with amphetamine and MA use than cocaine use

(Henning et al., 2019), probably because the short half-life of cocaine means that accumulating and sustaining high plasma concentration levels of that drug is difficult. Stimulant-induced psychosis has been reported after acute intoxication in relatively naïve people and occasionally after low doses. Original reports of the condition describe onset of psychosis following typically high doses (i.e., 100 to 300 mg of amphetamine; Henning et al., 2019).

The prevalence of stimulant-related psychosis is unclear, with studies on MA-induced psychosis reporting estimates ranging from 7 to 76 percent (Lecomte et al., 2018). A review of the literature suggests an overall rate of 36.5 percent among people using MA, with rates somewhat diverging based on whether MA use was lifetime (42.7%) versus current (22.1%; Lecomte et al., 2018). Fear regarding the stigma associated with psychotic symptoms and the persecutory nature of the altered perceptions of reality likely contribute to the inconsistent description of stimulant-induced psychosis.

The prevalence of psychosis induced by prescription stimulants is low. In adolescents and young adults taking prescription methylphenidate or amphetamine for ADHD, psychosis has been reported in approximately 1 in 660 patients, with amphetamine carrying a greater risk than methylphenidate (1.78 per 1,000 people per year versus 2.83 per 1,000 people per year; Moran et al., 2019). Although these rates are low, FDA added a warning label to these medications in 2007 that reads “stimulants may cause treatment-emergent psychotic or manic symptoms in patients with no prior history” (Moran et al., 2019, p. 1,129). This is especially true when prescription stimulants are injected or snorted.

The presence of stimulant-induced psychosis has implications for determining the appropriate level of care. Patients with stimulant-induced psychosis may require more acute psychiatric care, where there are staff to ensure patient safety. (Learn more about determining levels of care by reading Chapter 5.)

Development of stimulant-induced psychosis

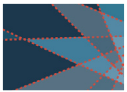
Some researchers and clinicians describe the development of stimulant-induced psychosis as an evolving process, dividing presentations of

stimulant-induced psychosis into three major categories: acute MA psychosis, chronic or persistent MA psychosis, and schizophrenia (Bramness et al., 2012; Deng et al., 2012). Acute stimulant-induced psychosis is directly related to the amount of substance used and lack of sleep of a specific binge. Persistent MA psychosis is related to the chronic use of MA, and patients tend to demonstrate more profound hallucinations, including visual, auditory, and tactile hallucinations.

Schizophrenia is a separate diagnosis from stimulant-induced psychosis, as the former is a substance-independent psychotic disorder. But a presentation of psychosis after stimulant use would warrant consideration of schizophrenia in the differential diagnosis to determine whether a stimulant use disorder–schizophrenia comorbidity exists. Use of stimulants in people with schizophrenia or schizoaffective disorder will likely exacerbate their psychosis; thus, patients may have a psychotic disorder like schizophrenia or schizoaffective disorder and stimulant use disorder simultaneously. Some patients may have co-occurring schizophrenia and present with positive and negative symptoms of schizophrenia after MA use, though this requires further study to determine the pattern of correlation.

Assessment of acute versus chronic stimulant-induced psychosis may be difficult and will likely require patients to engage in multiple treatment sessions. Patients should be evaluated after they have been able to sleep and regain some level of normal life functioning to differentiate between acute and chronic stimulant-induced psychosis. Patients who continue to experience hallucinations, altered perceptions of reality, and persecutory cues from their environment may be exhibiting chronic stimulant psychosis and may require longitudinal psychiatric intervention. Additionally, these patients may warrant diagnostic evaluation for a schizophrenia-spectrum illness. Persistent MA psychosis may occur with ongoing MA use, however, and requires medication treatment similar to that for schizophrenia (e.g., neuroleptics).

At first, people who use a moderately high amount of MA may experience intense curiosity about the world around them. This enthusiasm about “discoveries” changes, with time and increasing



doses, from “watching the world” to feelings of being watched. Behaviors become more fixed and stereotypic, culminating in intense suspiciousness and, in psychotic reactions, paranoid thinking and persecutory perceptions that misinterpret environmental cues. Visual hallucinations may be overreactions to barely glimpsed and recognizable objects in one’s peripheral vision or may be described as shadows of people or things. Auditory hallucinations similarly begin with hearing simple noises and usually progress to hearing others speak about oneself, typically derogatorily. In later stages of psychosis, the individual may have a persistently altered perception of reality and overwhelming feelings of being unsafe.

Manifestations of stimulant-induced psychosis

Although the symptoms of stimulant-induced psychosis mirror those of independent psychotic disorders (like schizophrenia), and heavy use of cocaine/amphetamines may precipitate schizophrenia, stimulant-induced psychosis and primary psychosis are distinct conditions (APA, 2013). DSM-5 criteria describe a substance-/medication-induced psychotic disorder as the presence of altered perceptions of reality (delusions) and/or hallucinations that occur during or soon after intoxication or withdrawal from a substance or shortly following exposure to a medication (APA, 2013). The symptoms cannot be part of a psychotic disorder and do not occur only during delirium. The substance must have the potential to cause altered perceptions of reality or hallucinations that result in clinically significant impairment. Per DSM-5, psychosis in the presence of substance use is considered a primary disorder when (APA, 2013):

- Symptoms substantially exceed what would be expected given the amount and type of substance taken.
- The individual has had previous non-substance-induced psychotic episodes.
- The onset of psychosis precedes the substance use.
- The psychosis lasts for at least 1 month after cessation of intoxication or withdrawal.

Presentation usually includes auditory and tactile hallucinations, paranoid thoughts, ideas of reference, and protective behaviors associated

with paranoia, all of which may lead to difficulties with social and occupational functioning (Glasner-Edwards & Mooney, 2014). Other often-reported psychotic symptoms include persecutory delusions, perceptions of jealousy, concerns of mind-reading, irritability, visual hallucinations, invasive thoughts, thought broadcasting, derealization, and depersonalization (Fluyau et al., 2019). Another common manifestation is stereotypy. As chronic, high-dose stimulant consumption continues, most people also withdraw from all social interactions and initiate other antisocial behaviors before intensive drug use culminates in paranoia or other symptoms of psychosis with limited insight.

Experimental studies in which participants received amphetamine or MA with variable doses/dosing schedules and with different routes of administration showed that, across all participants, only some people developed psychotic symptoms, the threshold dose was inconsistent, and the most common psychotic symptom was paranoia with ideas of reference (Glasner-Edwards & Mooney, 2014).

Risk factors for stimulant-induced psychosis include presence of ADHD, cognitive impairment, and certain neurobiologic factors (e.g., dysfunctions in the brain’s GABA systems; Bramness & Rognli, 2016). A family history of psychotic disorders (e.g., schizophrenia) may also be a risk factor.

The role of drug sensitization

Several issues pertaining to stimulant-induced psychosis are unresolved. There is some disagreement about the role of drug sensitization (kindling) in precipitating more frequent psychotic reactions at smaller doses than previously required and sooner after drug use is reinitiated following a period of abstinence (Rolland et al., 2011). There is also disagreement about the role of sensitization in deepening postwithdrawal depression. The mechanisms for this “reverse tolerance” are not fully understood.

Duration of stimulant-induced psychosis

Symptoms of acute stimulant-induced psychosis usually abate spontaneously with cessation of substance use. Symptoms of chronic or persistent psychosis may occur for 6 months or longer (Glasner-Edwards & Mooney, 2014), particularly among patients with a long history of severe MA

use. Hallucinations may stop within 24 to 48 hours of cessation of substance use, and paranoia and altered perceptions of reality decrease over the next week to 15 days. Clinicians also report that drug-induced psychosis dissipates more quickly for cocaine use—usually in 1 to 3 days—compared with up to 2 to 3 weeks for MA use. Resuming or continuing stimulant use, using other substances (including alcohol, when used heavily), and experiencing stress or lack of sleep can all trigger recurrence of psychosis after symptoms have resolved and after prolonged periods of abstinence (Glasner-Edwards & Mooney, 2014).

The duration of stimulant-induced psychosis is somewhat in dispute. Typically, uncomplicated psychosis induced by stimulants resolves rapidly unless more of the drug is taken. However, observational studies from Japan and Thailand suggest that MA-induced psychosis can persist well beyond the 1-month cutoff in DSM-5 and may become a more chronic condition, even in individuals without a previous psychiatric history (Glasner-Edwards & Mooney, 2014).

Treatment of stimulant-induced psychosis

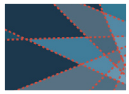
Treating a patient who presents with stimulant-induced psychosis entails rapid, systematic visual assessment, deescalation of agitated or paranoid

behavior, continued observation and monitoring, and symptom management. All unnecessary stimulation should be reduced, but complete sensory deprivation should be avoided. Ideally, the patient should be moved to a quiet hospital room with moderate lighting and sufficient space and staff should talk in a subdued manner and without rapid or unexpected movements. The clinician should try to calm the patient and provide reassurance that he or she is safe (Glasner-Edwards & Mooney, 2014; Holmwood & Gowing, 2019). Deescalation using the AGRO+ model may help engage the patient in a conversation, decreasing the patient's persecutory perceptions, and increasing the sense of safety and well-being (Holmwood & Gowing, 2019; Overdose Response Strategy, New England High Intensity Drug Trafficking Area, & Boston Medical Center Office Based Addiction Treatment Training and Technical Assistance, 2020). (See Exhibit 3.8.) It may be prudent to medicate patients who are nonresponsive to destimulation and deescalation using benzodiazepines and, if patients are unresponsive to initial benzodiazepine doses, antipsychotic medications. In rare instances, ketamine or similar medications may be appropriate in treating the patients' symptoms.

EXHIBIT 3.8. AGRO+ Method for Deescalation With Aggressive Patients

DEESCALATION				
A	G	R	O	+
Assess what triggered the agitation by calmly talking with the patient. Use a patient-centered focus.	Gauge your feelings about the situation. Be mindful that your verbal and nonverbal cues can escalate or deescalate the situation.	Respond calmly yet firmly to the patient. Stand at a safe distance in an open posture. Use open-ended questions and reflective listening.	Observe the patient's verbal and nonverbal cues. Are the deescalation techniques working?	Positive Reinforcement As the patient starts to deescalate, reinforce this desired behavior by offering something, like a glass of water or a snack.

Source: Adapted with permission from Hanieh et al. (2013).



Chronic/persistent stimulant-induced psychosis warrants referral for psychosocial intervention, like cognitive-behavioral therapy, SUD treatment to initiate abstinence and promote recovery, and the use of antipsychotic agents to treat the persistent symptoms of psychosis (Braunwarth et al., 2016; Glasner-Edwards & Mooney, 2014). Individuals with co-occurring stimulant use disorder and schizophrenia (or other psychotic disorder) may also benefit from case management and comprehensive care to address a broader range of potential service needs, like those pertaining to housing and vocational rehabilitation (Glasner-Edwards & Mooney, 2014).

The antipsychotics olanzapine, haloperidol, aripiprazole, risperidone, and quetiapine each may be useful in treating stimulant-induced positive and negative psychotic symptoms (Bramness & Rognli, 2016; Fluyau et al., 2019). Each medication carries unique side effects (e.g., metabolic syndrome caused by second-generation atypical antipsychotics, extrapyramidal symptoms [medication-induced movement disorders] caused by haloperidol). Prescribing decisions should be based on each patient's risk-benefit profile and reevaluated throughout the course of treatment (Fluyau et al., 2019).

Differential diagnosis of acute confusional states should include the possibility of head injury, intracranial hemorrhage, electrolyte imbalances, infection or medical comorbidity, acute trauma response, or thyrotoxicosis. Information from family and significant others is helpful, and toxicology testing may also help confirm a diagnosis (Glasner-Edwards & Mooney, 2014). Assessment tools like the Diagnostic Interview Schedule and the Composite International Diagnostic Interview can help differentiate between primary and stimulant-induced psychosis (Glasner-Edwards & Mooney, 2014).

Acute stimulant-induced psychosis should generally be managed in a hospital psychiatric department or similar facility. Minor psychotic episodes with low-grade symptoms that respond readily to neuroleptic medications may, on some occasions, be managed in a well-staffed, freestanding office-based addiction treatment program if sufficient

personnel with training and experience in treating co-occurring disorders are readily available. Urine testing is recommended to confirm a diagnosis of stimulant-induced psychosis because the syndrome can closely mimic other disorders that may have psychotic symptoms, such as medical comorbidities, schizophrenia, mania, depression, other substance intoxication states, or catatonia.

The criteria for placement should reflect the persistence of the condition, the competence and training of personnel, and the drug taken. People with MA use who have accumulated high plasma concentration levels from longer binges and larger doses of stimulants with longer half-lives may be more prone to protective behaviors during psychosis. This is especially likely if psychotic symptoms include paranoia about attempts to medicate them, which could lead to aggressive behavior and difficulty following medication instructions after release from the hospital.

Aggression and Violence

A potential problem associated with MA use is the risk of sudden and intense violence. Reports by law enforcement officials, psychiatrists, and people using these substances themselves link stimulants to aggression and unprovoked assaults. A causal link between aggression in humans and use of stimulants has yet to be consistently established (Kuypers et al., 2020). But research has shown a robust association between MA use and increased risk of violent behavior or being a victim of violence (Foulds et al., 2020; McKetin et al., 2020; Richards et al., 2019; Stoicescu et al., 2019). MA use and psychopathy traits and behaviors (e.g., aggression, violence, criminal acts) may be associated with corticostriatal abnormalities consistent with decision-making deficits, increased impulsivity, and addictive behavior (W. F. Hoffman et al., 2020).

Research suggests MA may be associated with aggression. Of individuals with MA use and with past violent behavior, 33 percent reported initiating MA use before first engaging in violent behaviors, and 12 percent first engaged in violent behavior during the same year they started using MA (Brecht & Herbeck, 2013). A study from New Zealand (Foulds et al., 2020) examined patients throughout

the life course and found an increased risk of both violence perpetration and violence victimization among people who used MA, suggesting that the population associated with violence is also a population that is disproportionately victimized.

Compared with MA, fewer studies have examined aggression and violence resulting from cocaine use (Kuypers et al., 2020). Cocaine may have some influence on impulsivity, but evidence for this is largely from animal studies, and human studies have been too inconsistently designed to yield firm conclusions (Kuypers et al., 2020). Among the small number of human studies reporting a link between aggression and cocaine use, acute cocaine use has been associated with violence resulting in injury (Chermack et al., 2010), youth violence (Stoddard et al., 2015), and—in women who inject drugs—violent criminal behavior (Butler et al., 2017).

Because drug-induced psychoses can increase the potential for violence in response to perceived persecution and resulting paranoia, sound behavioral management techniques to prevent this negative and dangerous response are essential.

For more information about how to manage violent behaviors in people with SUDs (with or without psychosis), see the Substance Abuse and Mental Health Services Administration's (SAMHSA) Treatment Improvement Protocol (TIP) 25, *Substance Abuse Treatment and Domestic Violence* (<https://store.samhsa.gov/product/TIP-25-Substance-Abuse-Treatment-and-Domestic-Violence/SMA12-3390>); TIP 36, *Substance Abuse Treatment for Persons with Child Abuse and Neglect Issues* (<https://store.samhsa.gov/product/tip-36-substance-abuse-treatment-for-persons-with-child-abuse-and-neglect-issues/SMA12-3923>); and TIP 44, *Substance Abuse Treatment for Adults in the Criminal Justice System* (<https://store.samhsa.gov/product/TIP-44-Substance-Abuse-Treatment-for-Adults-in-the-Criminal-Justice-System/SMA13-4056>).

Co-Occurring Disorders and Conditions

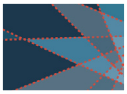
People with stimulant use disorders are likely to have one or more coexisting or preexisting disorders and conditions that can make differential diagnosis challenging or complicate treatment. Preclinical studies and some surveys seem to indicate that neurologic deficits associated with ADHD, neuroanatomical abnormalities, alcohol use disorder, posttraumatic brain lesions, and posttraumatic stress disorder (PTSD) may be correlated with increased vulnerability to stimulant use disorders.

People with MA use can experience co-occurring psychotic symptoms (e.g., paranoia, hallucinations), depressive disorders, anxiety disorders, polysubstance use (especially involving cannabis, benzodiazepines, and hypnotics), ADHD, gambling disorder, compulsive sex, sleep disorders, and eating disorders (Rawson, Ling, & Mooney, 2015). Cocaine use has been similarly linked to multiple psychiatric disorders, including ADHD, PTSD, bipolar disorder, antisocial personality disorder, eating disorders, insomnia disorder, and anxiety disorders (Butler et al., 2017; SAMHSA, 2020l).

The following sections describe some of the most common premorbid and co-occurring disorders and conditions among individuals who use stimulants, with some comments on treatment precautions.

Polysubstance Use

Concomitant use of a variety of other licit and illicit psychoactive substances is a common correlate of stimulant use. In a latent class analysis of more than 700 adults with past-month use of stimulants, four notable patterns of polysubstance use emerged: (1) high use of MA and cannabis but moderate use of alcohol and nonprescribed opioids; (2) high use of crack cocaine and alcohol but moderate use of cannabis; (3) high use of powder cocaine, alcohol, and cannabis but moderate use of crack cocaine; and (4) high use of crack cocaine, powder cocaine, nonprescribed opioids, alcohol, and cannabis but moderate use of MA, prescribed opioids, and



nonprescribed tranquilizers (Timko et al., 2018). Concomitant use of cocaine with benzodiazepines to blunt the dysphoric effects of the latter is also common.

Speedballing or goofballing—simultaneous use of an opioid and cocaine or other stimulant—is still prevalent in many places because the combination is perceived to smooth the effects of each drug. From 2011 to 2017, the number of people seeking opioid treatment who reported past-month MA use increased from nearly 19 percent in 2011 to 43 percent in 2017 (M. S. Ellis et al., 2018). From 2015 to 2017, the number of people with past-month heroin use who reported also using MA tripled from 9 to 30 percent, reflecting what some have termed a “twin epidemic” of opioid and MA addiction (Strickland et al., 2019).

In the 2009 to 2014 National Health and Nutrition Examination Survey, polysubstance use was common among people with current cocaine use (30 percent reported using one other substance, almost 31 percent reported using two, and 19 percent reported using three or more; Bahdila et al., 2020). Typically used substances were alcohol (almost 68%), tobacco (47%), cannabis (43%), prescription opioids (13%), MA (6%), and heroin (nearly 5%).

The combination of cocaine and alcohol is particularly dangerous. Researchers have established that cocaethylene, the ethyl ester of benzoylecgonine, forms in the liver when a person uses these two substances together. The person may experience more intense pleasure than if using either substance alone, but he or she is also exposed to the combined toxicities of cocaine and the even more potent cocaethylene (da Silva Maia et al., 2017; A. W. Jones, 2019; Liu et al., 2018).

Because cocaethylene has a longer half-life (2 hours) than cocaine (about an hour; A. W. Jones, 2019), the cumulative and additive effects found in the combination increase the incidence of lethal heart attacks and stroke (18 times higher risk of sudden death than with cocaine alone). Cocaethylene appears to prolong the duration of cocaine-related increases in blood pressure and, in turn, to increase the likelihood of small-vessel cerebral infarct or intracerebral hemorrhage.

Cocaethylene is particularly toxic to the liver and may be associated with increased risk of intensive care unit admission (Wiener et al., 2010). Cocaethylene has been detected in cases of cocaine-related sudden deaths that were attributed to drug toxicity as well as cocaine-related cases of violent death (i.e., gunshot wound, motor vehicle accident, suicide by hanging; Pilgrim et al., 2013). Fatalities involving cocaethylene may also be due to cerebral hemorrhage, stroke, other cardiovascular events, or hyperthermia (A. W. Jones, 2019). For people with chronic cocaine use, cocaethylene also increases the risk of experiencing panic and anxiety attacks, especially attacks that persist for some time.

The popularity of cannabis among people who use stimulants is explained by its pharmacologic properties. Because cannabis induces vasodilation of nasal mucosa, it attenuates the vasoconstriction of cocaine so that absorption is increased. Thus, co-use of cannabis and stimulants enhances their euphoric effects and, in MA use, decreases subjective dysphoric effects (Porcu & Castelli, 2017).

“Chemsex,” or the use of multiple substances to enhance sexual pleasure, is a potential health threat in polysubstance use with stimulant use (Giorgetti et al., 2017; Hammoud et al., 2018; Stevens et al., 2020; Torres et al., 2020). In particular, concomitant use of gamma-hydroxybutyric acid, alcohol, amyl nitrates, erectile dysfunction medications, and/or ketamine may be popular enhancements to the sexual experience, and each contributes differently to the potential for emergency intervention for patients.

Psychiatric Disorders

Research suggests that most people who use stimulants have concurrent mental disorders. Identified anxiety, phobias, ADHD, and antisocial personality disorder typically precede chronic cocaine use, whereas alcohol use disorder, depression, and paranoia generally follow stimulant use. For MA use, people appear more likely to have non-substance-induced, preexisting lifetime depressive, anxiety, or psychotic disorders than to have MA-induced depressive, anxiety, or psychotic disorders (Salo et al., 2011).

Differentiating co-occurring psychiatric disorders from stimulant-related disorders can be challenging. Acute or chronic stimulant intoxication can elicit symptoms of anxiety that are indistinguishable from phobias, obsessive compulsiveness, panic, and generalized anxiety. The parallels between symptoms of stimulant-induced psychosis and schizophrenia are discussed in the section “Stimulant-Induced Psychosis” earlier in this chapter. Withdrawal from stimulants can cause symptoms similar to major depression, resulting in symptoms like sad mood, fatigue, increased sleepiness, and thoughts of self-harm (UNODC, 2019b).

The prognosis for SUDs is worsened by the presence of other untreated psychiatric disorders (or polysubstance use). Patients with co-occurring SUDs and mental disorders need treatment for both; the psychiatric problems may or may not improve with reduction in use. Antidepressant and neuroleptic medications with low anticholinergic and sedative properties are preferred because of their low potential for addiction. Sedative–hypnotics and benzodiazepines must be used with caution in high-risk populations (e.g., older adults, people consuming alcohol, people with a history of prescription medication misuse; Guina & Merrill, 2018).

TREATING CO-OCCURRING MENTAL DISORDERS

People with stimulant use disorders also frequently experience other mental disorders or psychiatric symptoms, such as depression and anxiety. Patients with stimulant use disorder and any co-occurring psychiatric illness or symptoms should have both disorders treated concurrently rather than wait to address the mental health issue until after they are in recovery. Most mental disorders can be treated while the person is pursuing recovery. If clinicians delay in treating those co-occurring symptoms or disorders, it can put at risk the person's chances of achieving and staying in recovery from their stimulant use disorder.

Preexisting Medical Conditions

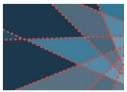
Any preexisting acute or chronic physical conditions are also likely to be complicated and exacerbated by the stress of stimulant intoxication and withdrawal. Particularly dangerous coexisting medical conditions include any history of seizures, coronary heart disease and other cardiac problems, thyroid problems, hypertension, or respiratory and pulmonary disease. Hypertension, renal failure, and possibly diabetes mellitus, which are risk factors for stroke, can be exacerbated by cocaine use (Goel et al., 2014).

Patients who are already taking medications for other medical conditions may be at heightened risk for serotonin syndrome when stimulants are combined with certain antidepressants or neuroleptics. Additional cardiovascular risk exists for patients prescribed beta-blockers who continue to use stimulants, particularly cocaine.

Traumatic Injury

People who use stimulants may be at an increased risk of traumatic injury. A review of studies looking at amphetamine-type substance use and associations with traumatic injury or death from motor vehicle accidents found a mixed association in terms of traumatic injury but a moderately positive association with death (Hayley et al., 2016). In one sample of more than 2,500 trauma patients admitted to a Level II trauma center between 2005 and 2015, 6.5 percent tested positive for MA and 5 percent for cocaine (Neeki et al., 2018). Traumatic brain injuries appear to be prevalent in people with cocaine and MA use disorder (Duong et al., 2018; Yeung et al., 2013) and should be managed with appropriate interventions based on the cognitive deficits identified in a neurologic evaluation (Ramesh et al., 2015).

Patients appearing in hospital EDs following mild to severe traumas may use stimulants and may have been involved in physical altercations or accidents. Among men reporting to the ED with traumatic injuries (Armenian et al., 2019), those who used stimulants had 2.9 increased odds of experiencing any violent injury and 3.3 increased odds of experiencing a penetrating injury (i.e., gunshot or stab wound).



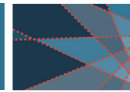
Stimulant use may be associated with not just an increased risk of traumatic injury but worse traumatic injury-related outcomes, such as mortality and healthcare resource use. A lifetime history of an SUD is associated with a significantly elevated mortality rate following inpatient discharge for traumatic injury (compared with people without lifetime SUDs); cocaine in particular has a 1.1 to 1.6 increased risk of all-cause mortality following discharge (Dezman et al., 2020). In individuals who sustain burn injuries, stimulant use is associated with longer hospital length of stay and a higher need for skin grafts, both of which suggest stimulant use may result in greater healthcare resource use (Hulsebos et al., 2020). In a survey of nurses, residents, and other faculty at a Level I trauma center, respondents largely agreed not only that patients who used MA tended to need more hospital resources and have a longer length of stay in the ED, but also that they required more effort on behalf of staff to treat and were perceived by staff to be more violent than patients who had not taken MA (Richards et al., 2019).

Sexual assault is also reported by an increasing number of both men and women who report stimulant use (Kittirattanapaiboon et al., 2017; Lutnick et al., 2015). Sexual assault while using stimulants is particularly problematic for women engaged in sex work for acquisition of the substance. Additionally, studies have examined the increased risk for intimate partner violence among both men and women who engage in regular stimulant use (Crane et al., 2014; Foulds et al., 2020; P. H. Smith et al., 2012). Clinicians should be familiar with appropriate places to which to refer patients to help them cope with trauma associated with sexual assault and intimate partner violence.

Linking Treatment Programs and Medical Facilities

Because the ED may be the first point of contact with the medical system and potential treatment for people with stimulant use disorders, hospitals need to give attention to establishing and supporting a continuum of care in which appropriate linkages among all necessary services and programs for these patients are present. The task of developing and encouraging these linkages among treatment components cannot fall to hospital staff alone; all providers and staff should be encouraged to cooperate in the effort. If not connected to the treatment system, people who use cocaine or MA will likely return repeatedly to the ED and other hospital departments for care of more and more serious health and mental health problems. Stimulant use disorders, like all SUDs, are lifelong, relapsing conditions that require ongoing management and support.

Hence, treatment programs should take primary responsibility for developing linkages with hospitals, using several approaches. The best approach is to have an SUD treatment practitioner or trained nurse/social worker visit the hospital and other medical facilities regularly to identify, screen, encourage, and follow up with patients who have stimulant-related and other substance use problems and need access to the ongoing treatment continuum. Peer recovery support specialists also can be found in hospital settings and can help link patients with acute SUD crisis to longer-term SUD services outside the hospital (see the text box “Connecting Patients to Peer Recovery Support Specialists”). A face-to-face visit by an outreach specialist or peer recovery support specialist is particularly effective in supporting the crisis-precipitated motivation to enter treatment, especially if the patient is hospitalized for some time. Because a crisis creates an intervention opportunity, the patient may be unusually receptive to considering lifestyle changes and the need for longer term treatment.



CONNECTING PATIENTS TO PEER RECOVERY SUPPORT SPECIALISTS

Medical providers can facilitate the recovery process for people taking stimulants by connecting them with a peer recovery support specialist. Also called a recovery coach, a peer recovery support specialist is an individual (or in the case of a family peer specialist, a close friend, family member, or other loved one of an individual) with lived experience with an SUD and recovery. These individuals carry out a wide range of recovery-related activities, such as mentoring or coaching people just entering recovery, facilitating and leading recovery groups, and connecting people just entering recovery to other recovery resources.

Research suggests that placing peer recovery support specialists in hospital settings is feasible and effective. For instance, Rhode Island's AnchorED program links patients presenting to the ED for opioid use disorder with peer recovery support specialists who provide naloxone kits and overdose education and who can connect these patients with more extensive community-based peer recovery support services as needed (Waye et al., 2019). Regardless of the type of setting in which a peer recovery support specialist works (e.g., hospitals, outpatient clinics, SUD treatment programs), use of peer recovery has been associated with improved outcomes, such as a greater likelihood of completing medically supervised withdrawal, reduced substance use, an increased likelihood of attending mutual-help programs (e.g., Narcotics Anonymous), reduced hospitalizations, fewer inpatient psychiatric or substance use-related readmissions, increased self-efficacy, and improved quality of life (Eddie et al., 2019).

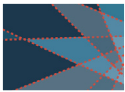
Not all medical facilities employ peer recovery support specialists. But if such individuals are available, medical personnel should become familiar with who they are, what they do, and how to connect them with patients.

It also may be realistic for hospital staff to provide patients with stimulant use a list of available treatment facilities for stimulant use disorders and/or other SUDs that is developed by the hospital's SUD treatment staff. However, patients in crisis may struggle to self-refer related to the fatigue, exhaustion, and depression associated with stimulant withdrawal and the persecutory perceptions of reality associated with acute stimulant use.

Some educational literature on stimulant use might also be helpful—particularly regarding withdrawal symptoms, stimulant-induced psychosis, and medical complications—if the patient or a significant other is willing to read it. Because hospital medical staff must know about the addiction process to understand patients whom they see every day, cross-training in the field of SUD treatment is vital for learning about and actively supporting the development and use of linkages and referral mechanisms. At least one-fourth of people treated in hospitals are thought to have some type of substance use-related problem.

Motivation for change is often difficult to determine in the individual. Health problems may, however, motivate an individual to move from contemplation to action (Prochaska et al., 1992). Healthcare personnel working with a patient hospitalized for an acute drug episode should emphasize strategies to keep the patient safe even when he or she is using substances. Motivational interviewing focuses on exploring and resolving ambivalence and centers on motivational processes within the individual that facilitate change. This evidence-based practice builds on the patient's strengths, which may be the most important component for patients to be able to initiate treatment for their stimulant use disorder (SAMHSA, 2020m).

Hospitals often deal with people with frequent, revolving use of hospital EDs or inpatient hospital beds because of medical or psychiatric complications resulting from their substance use. The financial burdens can be severe for these patients and, if the patients lack insurance, hospitals' costs of care may be unrecoverable. Collaborative arrangements between hospitals and local treatment facilities can allow for door-to-door SUD treatment.



Obtaining Consent for Treatment

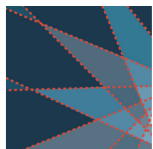
In obtaining the patient's consent for treatment, gathering information from others about the patient's history of substance use, making referrals for continuing care, or seeking reimbursement from insurance carriers, hospital staff must be familiar with the provisions of special federal laws and regulations for protecting confidentiality of SUD patient records as set forth in 42 U.S.C. §290dd-2 and 42 C.F.R. Part 2, as well as any applicable state laws and regulations. Patients who are intoxicated or psychotic may have diminished capacity for providing informed consent to treatment. If consent is obtained, even temporarily, from a relative, this may be considered a "disclosure of identifying information" and be subject to federal guidelines. In referring a patient from a hospital to an outside treatment program and making an appointment, staff are also making a disclosure and will ordinarily need a written consent form from the patient containing specified information.

Special exceptions apply to disclosing information in SUD patient records when medical personnel need this information to treat a medical emergency. However, the Part 2 regulations require that the SUD treatment provider document in the patient's record the nature of the emergency, what information was released, the name of the

person making the disclosure, and the date and time. For additional information about consent and confidentiality, see <https://www.samhsa.gov/about-us/who-we-are/laws-regulations/confidentiality-regulations-faqs>.

Summary

Patients who use cocaine or MA or who misuse prescription stimulants are at risk for multiple medical complications—some of which can have severe, long-lasting, or possibly even fatal consequences. The various routes of administration and pharmacokinetics of stimulants also play a role in the development of medical complications, as well as in the intoxication and withdrawal processes. Even SUD treatment providers who do not have medical training can benefit from knowledge about the medical risks of and treatments for cocaine use, MA use, and prescription stimulant misuse. These clinicians can play an important part in identifying symptoms and helping to connect patients with healthcare providers in a timely manner. Further, educating patients about the health consequences of stimulants might also help increase their motivation for engaging in and completing SUD treatment. (Chapter 4 discusses options for the nonpharmacologic treatment of stimulant use disorders in further detail.)



Chapter 4—Approaches to Treatment

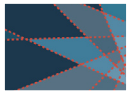
KEY MESSAGES

- Despite an increase in research into psychosocial treatments for people with stimulant use disorders, currently the only treatment with significant evidence of effectiveness is contingency management (CM).
- Other psychosocial treatments that have some support (especially if used in combination with CM) are cognitive-behavioral therapy/relapse prevention, community reinforcement, and motivational interviewing.
- There currently are no Food and Drug Administration-approved medications for stimulant use disorders, making it even more important that behavioral health and healthcare service providers understand and offer (or offer referrals for) CM or other psychosocial treatments.
- Other nonpharmacologic treatment approaches and strategies may also be useful for supporting recovery and improving health and well-being, including physical exercise, the Matrix model of neurobehavioral treatment, family or couples therapy, and mindfulness meditation.
- Clinicians need to promote harm reduction (e.g., through educating about needle exchange programs, offering naloxone, encouraging the use of fentanyl test strips) to people with stimulant use disorders who are not interested in formal treatment, because harm reduction techniques can help save lives.
- Many clinical management strategies have been developed to deal with clinical issues common in people with stimulant use disorders, like cognitive problems, intoxication issues, and co-occurring mental disorders.

During the early and mid-1980s, various unconventional remedies for substance use disorders (SUDs), including health foods, amino acids, hot tubs, electronic brain tuners, and other “New Age” treatments, emerged and disappeared. Research efforts to develop scientifically based treatments during this period often focused on behavioral techniques like contingency contracting (Anker & Crowley, 1982). Since these early efforts, an entire stimulant use disorder treatment literature has developed.

This chapter reviews the current state of knowledge on the treatment of people with stimulant use disorders, beginning with the approaches that have the most rigorous empirical support: contingency management (CM), cognitive-behavioral therapy (CBT)/relapse prevention (RP), community reinforcement, and motivational interviewing (MI). Other approaches with less support in the scientific literature are presented later in the chapter. These are physical exercise, the Matrix model, family or couples therapy, and mindfulness meditation.

Although at the time of this writing there are no Food and Drug Administration-approved medications with demonstrated clinical efficacy, an ongoing research program sponsored by the National Institute on Drug Abuse (NIDA) holds great promise for important treatment advances for stimulant use disorders.



ACCELERATING THE DEVELOPMENT OF STIMULANT USE DISORDER PHARMACOTHERAPIES

There currently are no Food and Drug Administration (FDA)-approved pharmacologic treatments for patients with stimulant use disorders. However, the National Institute on Drug Abuse's (NIDA) Division of Therapeutics and Medical Consequences (DTMC) helps advance such research through three programs targeted at SUD pharmacotherapies. DTMC supports the conduct of all clinical trial phases as well as assists with clinical trial design, trial implementation, and regulatory paperwork. Its pharmacotherapy programs are:

- The Pharmacotherapies Development Program: This program supports the development of novel medications and conducts safety and efficacy trials; stimulant use disorders involving cocaine and methamphetamine are high-priority areas given the lack of FDA-approved treatments for these conditions.
- The Addiction Treatment Discovery Program: Through preclinical testing, this program identifies, evaluates, and recommends potential medications as treatments for the medical management of SUDs.
- Regulatory Affairs Assistance for Medications Development Program: This program provides consultation on medication development regulatory requirements and strategies to federal agencies, NIDA grantees, and others. It also coordinates with FDA, filing the necessary regulatory documentation (like Investigational New Drug applications and Drug Master Files) as new medications enter or complete clinical studies.

For more on DTMC, including contact information for these programs, visit <https://www.drugabuse.gov/about-nida/organization/divisions/division-therapeutics-medical-consequences-dtmc/research-programs>.

How To Measure Effectiveness

This chapter reviews effective treatments for people with stimulant use disorders. To be judged effective, a treatment must have been tested and demonstrated to be effective in a randomized controlled trial (RCT). Many psychosocial and pharmacologic treatments have been investigated in such trials. Several psychosocial treatments for stimulant use disorders have proved effective, although no reliably effective pharmacologic treatments have been found to date. What has been learned so far about the use of psychosocial treatments for stimulant use is summarized below.

RCTs are the best available method for determining whether an intervention improves health. An RCT is a **prospective study** comparing the effect of some intervention against a control intervention in patients who are randomly assigned to the intervention group or the control group (Bhide et al., 2018).

In such trials, patients from a particular population sample (e.g., all admissions to clinic X during 2018 meeting a particular list of inclusion and exclusion criteria) who consent to participate are randomly assigned to the intervention under study or to a control condition. Random assignment helps

ensure against possible bias in assigning particular kinds of patients to the different groups and helps distribute evenly between the groups any participant characteristics that might influence outcomes.

Prospective means that researchers study the groups from the start of the intervention, as opposed to retrospectively compiling the information after the intervention is completed.

Retrospective observations are not RCTs but are still commonly used approaches to research. For instance, they are often used in studies relying on administrative claims and electronic health records databases. These studies tend to be less accurate because relevant information is not always available or may be distorted through reliance on people's recall. Having a comparison or control group is essential because most problems have some level of variability (i.e., they wax and wane over time) and because many health problems resolve over time without any formal treatment. The most effective way to determine whether any observed changes are due to the treatment being investigated rather than to natural variability is by comparing against a similar group of patients who either received no treatment or received a standard treatment.

Some of the alternatives to RCTs common in the SUD treatment field can provide useful information but have serious limitations that must be recognized. For example, following a group of patients who received a particular treatment in the absence of a comparison group can be informative in terms of characterizing what has happened to them (e.g., percentage who returned to use, percentage who received additional treatment, amount of change from pretreatment to posttreatment). However, such observations do not permit making any scientifically valid inferences about the role of the treatment provided in bringing about any of the changes observed during follow-up. For that purpose, a comparison group is necessary. Any changes observed might have

occurred in the absence of treatment. Without a comparison group, there simply is no way to rule out that possibility.

Similarly, when patients themselves select group membership, as opposed to being assigned by the researcher, one cannot make valid inferences about the role of treatment in the outcome. For example, comparing treatment completers to dropouts is common and may be informative in terms of characterizing how the groups fared, but it is not scientifically valid to infer that any differences observed between them were due to the different amounts of treatment received. Some other factor (e.g., differences in the amount of other demands on their time) could have been responsible both for the differential retention rates and for the subsequent differences observed at follow-up.

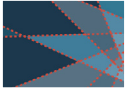
THE IMPORTANCE OF TEACHING HARM REDUCTION

Many people with stimulant use disorders will not be interested in formal treatment. But that doesn't mean that clinicians can't help them. Abstinence does not have to be the only goal for people with stimulant use disorders. Harm reduction techniques can teach people how to stop using stimulants or how to use them in a way that will reduce the risk of injury or death. Also, people can change their minds, and by "meeting patients where they are," rather than being argumentative and trying to force them into treatment, clinicians may find that patients who initially refuse treatment eventually become open to it.

Although harm reduction is not treatment, it can still help someone with a stimulant use disorder stay alive. Clinicians should never turn someone away from help simply because that individual isn't interested in entering formal treatment or pursuing abstinence.

Examples of harm reduction strategies that clinicians can use or share with patients are:

- **Educating them about or helping connect them to needle and syringe exchange programs.** People who use injectable drugs and who have reliable and trusted access to clean needles and syringes through a confidential exchange program may be less likely to share and reuse needles (Clarke et al., 2016). Exchange programs also help reduce the transmission of HIV (Des Jarlais, 2017).
- **Describing safer injection practices.** Teaching people who inject stimulants about proper injection techniques, handwashing and other basic hygiene, vein and wound care, and how and when to use antibacterial treatments can help reduce the risk of infection and other medical complications.
- **Distributing and educating on naloxone.** Naloxone is an FDA-approved opioid antagonist that reverses opioid overdose by helping people breathe normally (Office of the Surgeon General, 2018). Naloxone is not for stimulant overdose; it is an antidote to opioid overdose. But for people who use both stimulants and opioids, it can save their lives. Naloxone is not addictive and can be taken by injection or nasal spray.
- **Encouraging the use of fentanyl test strips.** Fentanyl, which can be deadly, may be added to drugs as a cheap filler. Fentanyl test strips allow individuals to determine before using drugs whether they have been mixed or cut with fentanyl. Use of the strips can reduce the risk of overdose.
- **Teaching patients HIV risk-reduction techniques,** like safer sex practices. People who inject stimulants are at risk for HIV and other blood-borne infections. Reducing risky sexual practices can help decrease their chances of contracting HIV and other sexually transmitted infections. As noted above, needle exchange programs also can help stop the spread of HIV.



Documented Psychosocial Treatment Approaches

The psychosocial interventions demonstrated to date to be efficacious in RCTs and other high-quality studies with people with stimulant use disorders share a common feature of incorporating well-established psychological principles of learning. Currently, these psychosocial approaches to treating people with stimulant use disorders have the most research support: CM, CBT/RP, community reinforcement approaches, and MI. Many studies look at combinations of these treatments. Thus, in making treatment decisions, clinicians should consider whether one of these approaches alone versus a combination of two might be best for a given patient.

It is impossible to quantify all aspects of psychosocial treatment or to account for all factors that affect patient outcomes. However, given that effective treatments and associated manuals are available, using them is prudent and helps ensure that patients receive the services that research has shown to be effective. An often-stated but unsubstantiated belief is that using a manual will limit or eliminate clinicians' flexibility and ability to exercise clinical judgment. A carefully prepared manual recognizes the importance of clinical judgment and flexibility in addressing the individual needs of patients and incorporates those features.

Contingency Management

CM is a well-known behavioral intervention designed to increase desired behaviors by providing immediate reinforcing consequences (in the form of incentives) when the target behavior occurs, and withholding those incentives when the target behavior does not occur. CM has been used with considerable effectiveness in treating individuals with a variety of SUDs and is very useful for treatment planning because it sets concrete short- and long-term goals and emphasizes positive behavioral changes (Benishek et al., 2014; Minozzi et al., 2016).

A meta-analysis found that CM had small and medium-sized effects on stimulant use at 3-month follow-up but not at 6 months (Sayegh et al., 2017). In a network meta-analysis of almost 7,000

participants across 12 different psychosocial interventions for cocaine and/or amphetamine use disorder, the combination of CM and community reinforcement approach was the most efficacious and most acceptable treatment in both the short and long term (De Crescenzo et al., 2018).

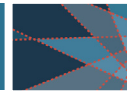
AshaRani and colleagues (2020) found that, across 44 studies of nonpharmacologic interventions for methamphetamine (MA) use, CM interventions showed the strongest evidence favoring the outcomes assessed, although tailored CBT alone or with CM was also effective in the target population.

Finally, H. D. Brown and DeFulio (2020) found that, across 27 studies looking at CM for MA use, nearly all (26 of the 27) reported reduced MA use.

Other positive outcomes across studies included longer retention in treatment, greater number of therapy sessions attended, higher utilization of medical and other services, reduced high-risk sexual behavior, increased positive affect, and decreased negative affect.

When considered collectively, CM interventions have by far the greatest amount of empirical support for their efficacy in promoting therapeutic behavioral change among people with stimulant use. In fact, interventions other than CM have demonstrated weak or nonspecific effects on stimulant use disorder-related problems (Farrell et al., 2019). People who use stimulants are sensitive to systematically applied CM interventions.

Like the other psychosocial interventions discussed in this chapter, CM may also be effectively used with other treatment approaches. In a review of 50 RCTs on 12 psychosocial interventions for cocaine or amphetamine use, CM plus community reinforcement was the only approach to result in increased rates of abstinence by the end of treatment, at short-term follow-up, and at long-term follow-up (De Crescenzo et al., 2018). This combination was also more effective than CBT alone, CM alone, CM plus CBT, and 12-Step programs plus noncontingent incentives. Treatment dropout rates were also lower with CM plus community reinforcement. These findings are consistent with those from other reviews that support CM (alone and in combination) as being highly effective for stimulant use disorders (Ronsley et al., 2020).



The size of the incentive may be important in generating positive outcomes, with higher-value cash incentives generally leading to more positive behavior changes (such as abstinence) than lower-value cash incentives (Stitzer et al., 2020). However, some research has found no difference in outcomes based on magnitude of incentive. For instance, Petry and colleagues (2015) studied differences in outcomes from standard-sized cash prizes (about \$300 on average) versus larger-sized cash prizes (about \$900 on average) in a CM program for people with cocaine use disorder and maintained on methadone. The two prize groups had no differences in drug-negative urine samples or duration of abstinence.

Pregnant women are an important subgroup for CM research. For instance, a study of women with cocaine use disorder who were pregnant or

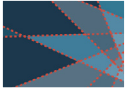
had young children found that CM is associated with longer cocaine abstinence and more cocaine-negative urine tests compared with use of noncontingency vouchers (Schottenfeld et al., 2011). For more information about stimulant use disorders in women who are pregnant, see Chapter 6.

Another population vulnerable to SUDs are individuals with serious mental illness (SMI). For SMI and stimulant use disorders specifically, McDonell et al. (2013) found that CM plus treatment as usual (mental health, SUD treatment, housing, and vocational services) was associated with fewer days of stimulant use and alcohol use and lower rates of injection drug use compared with treatment as usual. Researchers have also found CM added to usual treatment to be cost-effective (Murphy et al., 2016).

A WARNING ABOUT REIMBURSEMENT FOR CONTINGENCY MANAGEMENT

CM has the greatest weight of evidence supporting its use for the treatment of people with stimulant use disorders. However, Medicare and Medicaid currently limit the amount of money that can be used as an incentive in CM programs to a maximum of \$75 (Glass et al., 2020). Some states also have laws limiting CM payments. For instance, in Washington State, state-funded health insurance plans limit CM incentives to no more than \$100 (Glass et al., 2020). (Note, however, that CM incentives do not have to be monetary. Some programs use tokens, nonmonetary coins, or food, for example.)

Although some research in which CM has been successful has used much higher incentives—sometimes \$400 to \$500 per participant over the course of the study (Glass et al., 2020)—other studies have indicated CM effectiveness even when incentives were smaller (Hartzler & Garrett, 2016; López-Nuñez et al., 2016). Clinicians should be aware of current laws regarding CM payments and be prepared to offer other psychosocial interventions and services as needed.



WHAT CLINICIANS SHOULD KNOW ABOUT IMPLEMENTING CONTINGENCY MANAGEMENT

CM has a strong evidence base of support for treatment of people with SUDs generally, and stimulant use disorders specifically. But not all clinicians know or have been trained in CM and how to implement it. A walkthrough of this approach is beyond the scope of this Treatment Improvement Protocol, but the points below give important basic information about CM to help clinicians become more familiar with how to use it. The resources at the bottom of this text box offer more detailed guidance on this intervention.

- CM uses stimulus control plus positive incentives to achieve behavior change. This means as patients control their use of stimulants, they receive positive incentives (e.g., money) as incentives for their behavior. The common outcome targeted by the incentives is a stimulant-negative urine drug screen.
- Incentives come in the form of vouchers, points, or tokens that can then be exchanged for money, prizes, or privileges (like earning take-home doses of methadone for people in an opioid treatment program).
- Incentives can be administered regularly (called a fixed schedule), like every time the patient achieves a target behavior (e.g., remaining abstinent as documented by a negative urine screen), or they can be given intermittently (called a variable schedule; Kirby et al., 2016).
- Incentives can also be disbursed on an escalating schedule, with the incentive gradually increasing every time a target behavior is achieved. If a target behavior is ever not achieved, the incentive value “resets” back to the original value, and the escalating schedule begins again.
- A fishbowl procedure (also called variable magnitude of reinforcement) can be used to provide incentives on a variable schedule. In this approach, slips of paper are placed in a fishbowl—half indicating that an incentive has been won and half offering a reinforcing statement, such as “Good job!” This method prevents patients from predicting when they will and will not get an incentive.
- Some research suggests that people with SUDs respond better to CM that uses both immediate and delayed incentives, wherein patients earn an incentive right after meeting a target behavior but then also win the opportunity to potentially earn an even larger incentive in the future as the target behavior is continually met (Regier & Redish, 2015).
- Additionally, some research suggests that people with SUDs respond better to receiving concrete incentives—like an actual prize or money—rather than a voucher or token, which is only an incentive in the abstract and is not in itself valuable (Regier & Redish, 2015).
- To help maintain target behaviors, the longer a patient maintains a target behavior, such as remaining abstinent, the greater the incentive should be (Kirby et al., 2016). For example, a patient could earn more draws from the fishbowl for sequential stimulant-negative urine drug screens.
- Clinicians can work with patients to determine the schedule for giving incentives, such as right away or following a brief delay (e.g., giving vouchers that can be exchanged for prizes as soon as they have been earned, rather than at the end of the week) (Kirby et al., 2016).

Learn more about the major components of CM and how to implement it by reviewing:

- The Substance Abuse and Mental Health Services Administration’s Addiction Technology Transfer Center (ATTC) Network online course Contingency Management for Healthcare Settings (<https://attcnetwork.org/centers/northwest-attc/news/new-online-course-contingency-management-healthcare-settings>).
- The Motivational Incentives Suite—a collection of tools and other resources to help organizations understand and implement CM (<https://collaborativeforhealth.org/bettertxoutcomes/>).
- The ATTC Network’s guidance on the founding principles of CM (<https://attcnetwork.org/centers/network-coordinating-office/contingency-management-part-2-founding-principles>).

Cognitive–Behavioral Therapy/ Relapse Prevention

Despite the increase in research on CBT for stimulant use disorders over the past two decades, its effectiveness is still unclear (De Crescenzo et al., 2018; Ronsley et al., 2020). Nonetheless, many clinicians and researchers find CBT to be helpful. A Cochrane review from 2018 found mixed outcomes for CBT (including some positive findings, like an increase in percentage of abstinent days over a 90-day period and a reduction in symptoms). However, the review authors concluded that many CBT studies are small in size or poorly designed, making it difficult to have full confidence in their findings (Harada et al., 2018).

CBT in combination with CM may be especially helpful (De Crescenzo et al., 2018). One study reported that adding CM to CBT enhanced CBT's positive outcomes (e.g., cocaine-negative urine specimens) among people with cocaine use disorder (Carroll et al., 2016). Other researchers have found that CBT can have delayed positive effects on cocaine use disorder, with improvements appearing after study treatment has ended (Ronsley et al., 2020).

RP is a form of CBT that teaches patients strategies, skills, and lifestyle adaptations to help them change their thoughts and behaviors related to substance use. RP emphasizes (Hendershot et al., 2011):

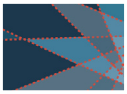
- Ways to cope with substance craving.
- Substance refusal and assertiveness skills.
- General coping and problem-solving skills.
- Strategies to prevent a full-blown return to use should an episode of substance use occur.

Carroll and various colleagues have adapted RP for cocaine use and demonstrated the efficacy of the adapted approach (Carroll, Rounsaville, & Gawin, 1991; Carroll, Rounsaville, Gordon, et al., 1994; Carroll, Rounsaville, & Keller, 1991; Carroll, Rounsaville, Nich, et al., 1994). In an initial study, RP was compared with interpersonal psychotherapy (IP), which teaches strategies for improving social and interpersonal problems (Carroll, Rounsaville, & Gawin, 1991). Retention was better with RP than IP, and trends suggested cocaine abstinence may have been as well, but that difference was not significant.

Using as a sample more than 300 individuals who had completed outpatient SUD treatment for people with stimulant use disorders, Farabee, McCann, and colleagues (2013) assessed 14 RP strategies designed to help with abstinence maintenance at baseline and 3-month and 12-month follow-up. They found avoidance strategies to be the most effective predictor of drug-free urines at all time points assessed. The strategies significantly correlated with negative urine screens at all time points were:

- Reducing use of other drugs.
- Avoiding friends with active drug use.
- Avoiding places where drugs are available.

Participating in 12-Step meetings significantly predicted negative urines at baseline and 12-month follow-up. (For more information about 12-Step and other mutual-help programs, see Chapter 5.)



THE PREVENTION AND TREATMENT OF PRESCRIPTION STIMULANT MISUSE

Prescriptions for stimulant medication for attention deficit hyperactivity disorder (ADHD) have been increasing over the last two decades, likely in part because ADHD diagnoses in children and adolescents have been increasing (Colaneri et al., 2017; Visser et al., 2014). As rates of stimulant prescriptions have increased over the last 20 years, so too have rates of prescription stimulant misuse, including diversion (Holt et al., 2020). Adolescents and college-aged young adults are particularly at risk for behaviors like feigning ADHD symptoms to acquire a prescription, taking ADHD medication to improve academic performance, or giving away their prescribed medication to others (Colaneri et al., 2017; Weyandt et al., 2016). However, it is not just adolescents and college students who are at risk for prescription stimulant misuse. Adults older than 19 years received more than half (55%) of all U.S. stimulant prescriptions in the last decade (Arria & DuPont, 2018). Although most people prescribed stimulant medications do not misuse them and a much smaller percentage have a diagnosable stimulant use disorder, misuse can and does occur (Arria & DuPont, 2018) and can have serious health and legal consequences (L. Y. Chen et al., 2016; Colaneri et al., 2017).

Clinicians should ensure that patients meet the established criteria for ADHD in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) to avoid writing unnecessary prescriptions for stimulant medications. If the patient meets DSM-5 criteria for ADHD and a prescription stimulant is deemed an appropriate treatment, the prescribing provider should cross-reference the prescription information with available data in state-run prescription drug monitoring programs. This step should be completed each time a prescription is provided.

In the absence of published randomized controlled trials or randomized clinical trials on the treatment of prescription stimulant misuse, treatment should follow the same path as for cocaine use or MA use. That is, patients with prescription stimulant misuse should be offered CM, if available. Research into CM for youth with SUDs shows these interventions can help increase the chances of abstinence in the short term (Stanger & Budney, 2019). Such interventions may be particularly helpful given that most people with past-year prescription stimulant misuse are younger than 26 (SAMHSA, 2020g). However, there is a lack of long-term research showing whether substance-related outcomes persist over time and which factors might help improve short- and long-term efficacy (Stanger & Budney, 2019). If CM is not available, evidence-based treatments such as CBT/RP, community reinforcement, and MI can be offered to patients misusing prescription stimulants.

Research has examined the effectiveness of social influence resistance strategies to help prevent diversion of stimulant medication in young adults. Holt et al. (2020) surveyed more than 1,500 college undergraduates to learn whether students found such strategies useful. The strategies consisted of students directly refusing to divert their stimulant medication, coming up with excuses to avoid diverting (“I don’t have any [medication] with me right now”), coming up with an alternative to diverting their medication (e.g., offering the person an energy drink instead), attributing their unwillingness to divert to an internal source (“I am not comfortable sharing my medication”), and blaming their unwillingness to divert on an external source (“My parents keep track of my prescription because they send it to me, so I can’t share any”).

In the study, 19 percent of the students said they had engaged in nonmedical use of prescription stimulants (i.e., prescription stimulant misuse) at some point during their time in college (Holt et al., 2020). Internal and external strategies were perceived as being the most helpful, and the use of excuses was rated the least helpful. Students who had previously engaged in diversion found the strategies overall to be less effective than did students at low risk for diversion. Clinicians working to prevent diversion in their patients not already diverting medication—as well as clinicians helping patients who are already diverting learn how to stop—might want to emphasize teaching refusal skills based on internal and external blaming strategies. Using these strategies may prove more effective than simply telling patients that they need to “learn to say ‘no’” when approached by someone wanting them to divert their medication.

Continued on next page

Continued

Clinicians can also help reduce diversion by checking prescription drug monitoring databases and checking urine drug screens. Other stimulant diversion prevention techniques include (Colaneri et al., 2017):

- Developing medication contracts that include the risks and benefits of the stimulant medication, the risks of misusing the medication, an agreement that the patient will only take the medication as prescribed, conditions for determining adherence (e.g., pill counts), and consequences of the patient violating the contract.
- Providing materials that educate patients about the dangers of misusing prescription stimulants (e.g., the risk of potentially harming people with preexisting heart disease or cardiac structural abnormalities).
- Prescribing a smaller number of pills.
- Prescribing long-acting formulations rather than short-acting formulations.
- Conducting periodic pill counts.
- Learning about and prescribing nonstimulant medications instead of stimulants.

Clinicians should also build linkages with local SUD treatment providers (including ones specializing in working with adolescents and young adults), so they can refer patients in need of formal treatment and services. Finally, clinicians should be sure to conduct SUD assessments for patients who are prescribed stimulants (even if the patient is not misusing the prescription stimulant) and refer patients for SUD treatment as needed. People taking prescription stimulants—even lawfully and as prescribed—are vulnerable to tobacco, cannabis, cocaine, hallucinogen, and opioid use (Arria & DuPont, 2018; Compton et al., 2018). (See Chapter 2 for more information about stimulant use disorder assessment.)

Community Reinforcement Approach

Community reinforcement is an individualized treatment designed to promote key lifestyle changes that are conducive to successful recovery (see Meyers & Smith, 1995; Sisson & Azrin, 1989):

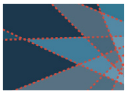
- Patients with partners/spouses who do not use stimulants are offered marital therapy to improve the quality of their relationships in a reciprocal and rewarding manner.
- Patients who are unemployed, employed in jobs that are high risk for substance use, or need vocational assistance for some other reason receive help in that domain.
- Patients are counseled and assisted in developing new social networks and recreational practices that promote and support recovery. Mutual-help group participation is not mandatory but is often used as an effective means of developing a new social network.
- Various types of skills training are provided depending on individualized patient needs, including substance refusal and associated skills, social skills, time management, and mood regulation.

- Patients with alcohol use disorder (AUD) and no medical contraindications are offered a program of disulfiram therapy coupled with strategies to support medication compliance.

Very few recent studies have examined community reinforcement alone, so it is unclear whether this approach delivers better substance use outcomes than other psychosocial approaches or usual care (Ronsley et al., 2020). One study of community reinforcement did find increased treatment retention and abstinence and decreased addiction severity after 24 weeks (De Giorgi et al., 2018).

More recently, research on community reinforcement has focused on the effectiveness of adding it to CM (Ronsley et al., 2020). When used together, these treatments appear to (De Crescenzo et al., 2018):

- Do a better job than usual care at retaining individuals in treatment.
- Do a better job than noncontingency-based approaches (either used alone or with 12-Step programs) at helping people achieve abstinence.
- Have better patient acceptance than treatment as usual.



In one review, community reinforcement combined with noncontingent vouchers was less effective at achieving abstinence from cocaine than was community reinforcement combined with CM (Schierenberg et al., 2012).

Motivational Interviewing

MI has been found to be an effective evidence-based, group- or individual-based treatment for people with SUDs, especially AUD (SAMHSA, 2019). MI and motivational counseling, as applied to SUDs, have been associated with decreased substance use, improved SUD treatment retention, lower rates of relapse, and better adherence to HIV risk-reduction behaviors (SAMHSA, 2019).

Recent studies of MI alone for stimulant use disorders show mixed results, with some finding no benefit and others finding improvements in reducing the number of days of cocaine use (De Giorgi et al., 2018). Intensive MI designed specifically for MA use disorder demonstrated no different outcomes in MA use or in anxiety compared with an education control group that also received MI, although it was nonintensive (Polcin et al., 2014). A Cochrane review of psychosocial interventions for stimulant misuse (Minozzi et al., 2016) included five studies comparing MI with no intervention. In these

studies, receiving any psychosocial treatment (including MI) was associated with better treatment retention and greater abstinence than no treatment at all. However, the authors noted a fair amount of bias and study design problems across all of the studies in their review, including those pertaining to MI. Thus, results should be interpreted with caution.

Recent studies on combining MI with other treatment approaches were either inconclusive or had unreported results. One review noted that MI combined with CBT has yet to demonstrate reliable improvements over other treatments (De Giorgi et al., 2018). However, some individual studies have reported good results from adding MI to CBT.

In a sample of military veterans with SUDs, MI combined with CBT or combined with CBT and continuing care both showed significant decreases in substance use (including cocaine use) and reductions in aggression compared with treatment as usual (Chermack et al., 2019). MI added to CBT tailored to the unique needs of gay and bisexual men who are HIV positive was associated with lower MA use, better HIV medication adherence, and reduced risky sexual behavior (i.e., having sex without condoms) over the course of 12 months (Parsons et al., 2018).

THE ROLE OF TELEHEALTH IN TREATING STIMULANT USE DISORDERS

Technology use continues to grow as more people rely on smartphones and other electronic devices for access to information, social connection, and work-related activities. Telehealth is the use of technology to support and enhance healthcare delivery. Telehealth includes online education materials and treatments, mobile applications, and synchronous audiovisual services.

Research has shown that telehealth can be a useful and cost-effective tool for people with SUDs (Dallery et al., 2019; Murphy et al., 2016; Tait et al., 2015). Although more research is needed on the use of telehealth for people with stimulant use disorders specifically, research on telehealth for SUDs in general or other substances specifically can still provide useful insight into how these innovative tools and approaches may be effective and beneficial for patients.

Examples of ways that telehealth can help clinicians and their patients include:

- Supporting formal treatment.
 - Self-guided web-based interventions using techniques from CBT and motivational enhancement have shown promise in increasing help-seeking and reducing role impairment for people using amphetamine-type stimulants (Tait et al., 2015).

Continued on next page

Continued

- In 2017, a mobile application, reSET, became the first prescription-based digital therapeutic cleared by FDA. The program is based on the community reinforcement approach model and allows physicians to prescribe an 84-day access period by providing a code required for download. A multisite clinical trial of more than 500 adults with an SUD (including stimulant use disorder) who were engaged in outpatient treatment and who used the reSET application had lower dropout rates and higher abstinence rates (FDA, 2017).
- Posttreatment telephone contact, whether structured or directive, is associated with perceived decreases in life events that contribute to substance use among people who use stimulants (Farabee, Cousins, et al., 2013). High dropout rates during treatment for stimulant use disorders suggest there may be utility to using telephone contact during treatment to encourage retention as well (Lappan et al., 2020).
- Reaching rural and underserved communities.
 - Telehealth can address barriers to receiving substance use treatment in rural communities, such as privacy concerns, lack of provider availability, and lack of evidence-based, culturally appropriate services (Lin et al., 2020; SAMHSA, 2016). Although promising, clinicians should be aware that patient-level barriers, such as reliable access to the Internet and devices that support audiovisual conferencing or mobile applications, may affect telehealth implementation (Hser & Mooney, 2021; Kleykamp et al., 2020).
 - Studies of people with alcohol, tobacco, and opioid use disorders show that telehealth can effectively promote treatment engagement and retention, perceived support from providers, and substance use reduction through increased access (Kruse et al., 2020; M. C. Mahoney et al., 2018; Weintraub et al., 2018). Research is needed to determine whether these benefits translate to people with stimulant use disorders.

Treatment Approaches With Supportive Research

Physical Exercise

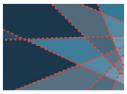
Physical activity is an area of robust and fast-growing research for therapies for stimulant use disorders. Aerobic exercise has been an increasing focus of SUD treatment studies broadly (as an add-on therapy, not as the lone treatment), including studies on stimulant use disorders (Sanchez et al., 2017). A review of physical activity interventions for people with MA use (Morais et al., 2018) found that, compared with nonexercise intervention controls, improvements were observed for:

- Aerobic performance.
- Muscle strength and endurance.
- Body composition.
- Heart rate variability.
- Depression.
- Anxiety.

- MA use.
- MA cravings.
- Inhibitory control.

Other researchers have similarly found that structured aerobic exercise and resistance training help reduce depression and anxiety in MA use disorder (Morris et al., 2018; Rawson, Chudzynski, Gonzales, et al., 2015), which may be useful in helping patients remain in treatment and sustain abstinence.

A study by Rawson, Chudzynski, Mooney, et al. (2015) found that participants with a lower severity of MA use assigned to an exercise intervention reported fewer days of drug use and had fewer positive urine screens, compared with participants with a lower severity of MA use who received a health education intervention. In the STimulant Reduction Intervention using Dosed Exercise (STRIDE) study (Trivedi et al., 2017), a 12-week dosed exercise intervention in residential SUD treatment settings was associated with a



significantly higher percentage of days abstinent compared with a health education intervention. (Both interventions were add-ons to treatment as usual.)

Benefits of physical exercise to people who use stimulants may include enhanced antioxidant mechanisms, reduced oxidative stress, and decreased reward-seeking behaviors (Morais et al., 2018). Evidence from human trials of exercise for stimulant use indicates an improvement in neurotransmitter systems that become deranged with cocaine or MA exposure (especially dopaminergic systems; Morais et al., 2018). Exercise by people using MA may help increase their striatal D2/D3 receptor availability (Morais et al., 2018). Preliminary data suggest that exercise for MA use disorder may also lead to better MA-related outcomes by increasing dopamine receptor binding in the brain (Robertson, Ishibashi, et al., 2016).

The Matrix Model

The Matrix model (originally referred to as the “neurobehavioral model”) is a manualized outpatient treatment approach that was developed during the mid-1980s for the treatment of individuals with cocaine and MA use disorders (NIDA, 2018a). The model integrates treatment elements from a number of specific strategies, including RP, MI, psychoeducation, family therapy, and 12-Step program involvement. The approach’s basic elements consist of a collection of group sessions (early recovery skills, RP, family education, and social support) and individual sessions, along with encouragement to participate in 12-Step activities (NIDA, 2018a; Rawson, 2010).

In seven research projects evaluating the treatment model, application of the model was shown to be associated with significant reductions in cocaine, MA, and other substance use (Rawson et al., 1993; Shoptaw et al., 1994). Treatment participation in the Matrix model has also been demonstrated to be associated with a significant improvement in psychological symptoms and significant reduction in risky sexual behaviors associated with HIV transmission (NIDA, 2018a). Adaptations of the Matrix model are available to address the unique treatment needs of women with stimulant use

disorders in such areas as trauma, pregnancy and parenting, body image, and sexuality (SAMHSA, 2012).

Family and Couples Therapy

People with SUDs often have extensive marital, relationship, and family problems. Stable marital and family adjustment is associated with better treatment outcomes. Including family members in treatment is based on the view that they can provide important support for the patient’s efforts to change and offer additional information about the patient’s substance use and other behavior. Interventions directed at improving marital and family adjustment have therefore been judged to have the potential to improve treatment outcomes. Studies with people with AUD have supported this hypothesis, at least in part (Klostermann et al., 2011). Few studies have focused on stimulant use, however.

Research on family and couples therapy for stimulant use disorders is scant, but outcomes appear promising. In a study of women with SUDs who have children, family systems therapy was associated with a reduction in both likelihood of cocaine use and frequency of use over time, and, compared with control participants, a faster decrease in frequency of cocaine use over time (Slesnick & Zhang, 2016).

For more information about providing family and couples therapy for people with SUDs, see SAMHSA’s Treatment Improvement Protocol (TIP) 39, *Substance Use Disorder Treatment and Family Therapy* (<https://store.samhsa.gov/product/treatment-improvement-protocol-tip-39-substance-use-disorder-treatment-and-family-therapy/PEP20-02-02-012>).

Mindfulness Meditation

Mindfulness-based interventions have gained popularity as potential tools to help prevent return to use by people with SUDs (Chiesa & Serretti, 2014). Mindfulness-based psychotherapy for people with cocaine use disorder (Dakwar & Levin, 2013) resulted in a 73-percent treatment completion rate and a 55-percent abstinence rate.

Among people with stimulant use disorders who received 12 weeks of CM, concurrent use of mindfulness-based RP was associated with greater reductions in depressed mood, greater reductions in Addiction Severity Index score, and lower odds of stimulant use compared with a health education control group (Glasner-Edwards et al., 2017). Close to half the sample had major depressive disorder (43%), and approximately one-quarter had generalized anxiety disorder (24%). Compared with CM plus health education, CM plus mindfulness RP was associated with lower scores of negative affect, greater reductions in depression severity and psychiatric symptom severity, and—among people with depressive and anxiety disorders—decreased stimulant use (Glasner-Edwards et al., 2017).

A residential mindfulness-based intervention for women with SUDs (most of whom had amphetamine/MA use) similarly showed greater chances of treatment completion compared with the control condition. Also, program attendance significantly correlated with improvements in mindfulness, distress tolerance, and mood (D. S. Black & Amaro, 2019).

Mindfulness-based RP combined with a single dose of ketamine was associated with longer cocaine abstinence than mindfulness plus midazolam in a 2019 study by Dakwar and colleagues. The mindfulness-ketamine participants were also 53 percent less likely to return to use and had significantly lower scores on craving.

Case Management and Coordinated Care

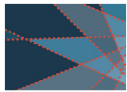
Case management and coordinated care are SUD treatment approaches with strong support, especially in terms of their ability to link people with SUD treatments and services and to retain patients in treatment (Vanderplasschen et al., 2019). These approaches are person centered and help ensure that care delivery is organized and includes all needed interventions and services, to the extent possible.

A small but promising line of research has looked at case management or coordinated care specifically among people with stimulant use disorders:

- In a pilot study, a strengths-based case management intervention for people with HIV who used injection drugs or smoked crack cocaine was associated with a decrease in detectable viral load (Kral et al., 2018).
- A study of women who used crack cocaine found case management was associated with improvements in drug and alcohol use (i.e., lower frequency of use), mental and emotional health (e.g., less depression or anxiety), and employment (Corsi et al., 2010).
- Men and women who were receiving public assistance and had a long history of substance use (including cocaine use) benefited from a coordinated care management approach designed to help link patients to SUD treatment, provide them with SUD-related services, and help them find employment (Morgenstern et al., 2009). Compared with the usual care group, women (but not men) in the program saw an increase in employment over time.

Vocational services are an important part of case management and coordinated care approaches; they can help people with SUDs, including stimulant use disorders, reintegrate into the workforce, learn valuable skills, and earn wages. Employment is an important aspect of long-term recovery and is associated with successful SUD treatment completion and 6-month abstinence (Sahker et al., 2019). Case management and coordinated care that incorporate vocational training or employment assistance may improve patients' chances of stopping stimulant use and staying in recovery following treatment.

For instance, the Compensated Work Therapy (CWT) program is a Department of Veterans Affairs clinical vocational rehabilitation service that supports veterans in finding and retaining employment. CWT interventions have been combined with CM to help veterans with SUDs not only improve employment outcomes but reduce substance use (Cosottile & DeFulio, 2020). Employment-based CM programs have been particularly successful for patients with cocaine use and opioid use disorders (OUDs; Cosottile & DeFulio, 2020).



For more information about vocational services, see SAMHSA's TIP 38, *Integrating Substance Abuse Treatment and Vocational Services* (<https://store.samhsa.gov/product/TIP-38-Integrating-Substance-Abuse-Treatment-Vocational-Services/SMA12-4216>), and SAMHSA's *Advisory, Integrating Vocational Services Into Substance Use Disorder Treatment* (<https://store.samhsa.gov/product/integrating-vocational-services-substance-use-disorder-treatment/pep20-02-01-019>).

Although case management and care coordination is still a growing area of research, these positive findings, along with the research showing support for case management and coordinated care for SUDs in general, suggest that using these approaches, when possible, can help patients benefit further from treatment, even in non-SUD outcomes (like employment and HIV status).

Other Interventions With Supportive Research

Evidence on transcranial magnetic stimulation (TMS) suggests this could be a safe and effective treatment for people with SUDs, although this research area needs further study. TMS involves nonsurgical stimulation of the brain through magnetic electrodes placed on the scalp. It is painless and noninvasive. It is thought to work on SUDs in part by increasing dopamine delivery to certain parts of the brain (e.g., the limbic system) and by reducing impulsivity/increasing self-control mechanisms in the prefrontal cortex network.

Repetitive TMS (rTMS) has been shown to be effective in reducing cravings in AUD (De Sousa, 2013). A review of six studies looking at rTMS for cocaine use disorder found a reduction in cravings and an increase in cocaine-free urine screens but noted that the evidence is still preliminary and needs to be replicated in larger studies (Bolloni et al., 2018). Data also suggest that only high-frequency rTMS (rather than low frequency) is effective in reducing cocaine, amphetamine, or MA craving (Ma et al., 2019).

Other Models of Psychosocial Treatment

Network Therapy

Network therapy is based on the theory that people can recover from SUDs if they have a stable social network to support them in psychotherapeutic treatment. In this model, a patient receiving individual psychotherapy develops a network of stable, nonsubstance-using support people, such as family, a partner, and close friends. These support people learn strategies from the clinician to support the therapeutic process for the individual being treated. They may interact regularly with the clinician, participate in treatment sessions with the patient (SAMHSA, 2020k), and be involved in setting up treatment plans for the patient.

Inpatient (or Hospital-Based) Treatment

"Inpatient treatment" is a broad term encompassing the highest levels of medical care for patients who may be experiencing acute medical or psychiatric needs secondary to recent use of substances or acute withdrawal. Specifically, acute treatment services may involve 24-hour medical management or medical monitoring, particularly in instances where stimulant use has led to life-threatening medical problems, such as rhabdomyolysis, significant electrolyte imbalances, or severe cases of sleep deprivation.

Historically, inpatient treatment began in the 1800s for patients experiencing severe AUD in an attempt to reduce the community-level concerns related to uncontrolled alcohol consumption. Programs like the Washingtonian Home in the city of Boston were specifically designed to help patients detoxify from alcohol and return to society (White, 2004). Over time, these programs shifted to hospital-based or medically monitored care to reduce the morbidity and mortality associated with alcohol withdrawal.

Inpatient treatment for AUD traditionally consisted of a 28-day stay in a hospital or residential treatment facility, during which daily activities such as group psychotherapy and relaxation practice were provided in a structured format. Generally supportive and sometimes confrontational

in nature, inpatient treatment was aimed at detoxifying patients, combating their denial, and beginning the process of engaging with mutual-help programs.

The 28-day standard treatment regimen also became common for patients experiencing other SUDs. It was especially widespread in the early 1980s, when the numbers of patients seeking treatment for cocaine use disorder began to rise dramatically. Most of these inpatient programs for treating cocaine use were adapted with few or no modifications from the alcohol regimens and with little input from empirically based research. Such inpatient programs were called into question by insurance providers, and subsequently, their use steadily declined (Malcolm et al., 2013).

Today, acute treatment programs, colloquially referred to as “detoxes,” may admit patients for between 3 and 10 days for observation during initial cessation of substance use and restoration of physiologic homeostasis (the body’s natural ability to maintain critical functions, like normal core temperature and normal blood glucose levels) after significant periods of severe substance use. Acute treatment services vary greatly in the amount of recovery support available to patients and the number of medical staff onsite for the care and monitoring of patients.

Patients with significant medical or psychiatric comorbidity may be voluntarily admitted to medically or psychiatrically managed SUD care, often referred to as “Level 4 facilities” after the level that is assigned in the American Society of Addiction Medicine’s (ASAM) levels of care (ASAM, 2015b; K. Hartwell & Brady, 2018). These hospital-based residential programs are capable of accommodating the highest acuity patients and are used for acute stabilization of medically or psychiatrically complex patients.

Clinical stabilization programs, or transitional support services, are inpatient programs for patients with fewer medical or psychiatric comorbidities. These programs typically offer more recovery services for patients, including mutual-help groups, therapeutic communities (TCs), education or therapy groups, individual counseling, a therapeutic milieu, and other integrated

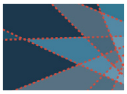
psychosocial services (ASAM, 2015b). These programs may last anywhere from 2 to 4 weeks (and often longer) and because of their extended nature may be the most beneficial in monitoring patients in early recovery from stimulants.

Special considerations should be made in treatment plans for patients experiencing stimulant withdrawal in inpatient settings (Braunwarth et al., 2016). Given the profound fatigue and excessive sleeping that can occur, considerations for exemptions from therapeutic sessions and educational services should be considered.

Nutritional support for patients recovering from SUDs is vital (Szydlowski & Amato, 2017). Increased access to high-calorie foods and foods with increased nutritional value may help in augmenting patients’ weight and correcting electrolyte imbalances (Braunwarth et al., 2016). Programs should consider consultation with appropriate nutrition or dietary specialists when necessary.

Additionally, given the possibility of increased depressive symptoms throughout acute withdrawal from stimulants, patients should be assessed for changes to risk for self-injury or self-harm regularly while in the inpatient unit, and safety plans should be in place in case patients develop thoughts of self-harm or self-injury. Suicide has been shown to be a significant cause of mortality for individuals who misuse stimulants (Butler et al., 2017; Farrell et al., 2019; Marshall & Werb, 2010).

Legislation regulating involuntary commitment to inpatient treatment settings (also known as mandated treatment) for SUDs varies throughout the United States. Many states have enacted legislation that allows clinicians or, in some instances, family members to file petitions for involuntary assessment of SUDs when patients are unable to adequately care for themselves or they pose serious risks to themselves or others. A judge may dismiss the petition or issue a court order for SUD treatment. Patients can choose to refuse treatment and ignore court orders, which may result in undesirable legal consequences. For patients admitted for involuntary treatment, special consideration should be given to identifying the reason for the involuntary commitment and the best strategy to mitigate that condition.



Involuntary treatment may be confrontational initially, and staff generally use MI techniques to elicit change talk and capitalize on patients' mandated treatment status. In the setting of involuntary treatment, it is vital to establish referral partners for when the patients have completed their requisite amount of time in SUD treatment.

Inpatient treatment varies in both insurance coverage and credentialing of staff. It is important to understand the nuances of different inpatient treatment programs, especially the duration of treatment, the medical/psychiatric credentials of the staff, and the program's ability to collaborate with outpatient treatment partners (Office of the Surgeon General, 2016). Given that stimulant use disorders are chronic, relapsing conditions, treatment should not end once patients leave an inpatient setting. These patients should always be "stepped down" into outpatient care.

In the past two to three decades, more patients have received primary SUD care in outpatient settings rather than inpatient treatment facilities. As this shift continues, inpatient treatment will remain reserved for patients experiencing the most severe forms of an SUD, with the highest risk of morbidity or mortality related to their medical or psychiatric presentation while using or stopping their use.

Residential Treatment

Residential treatment may be indicated for people with SUDs who need more structured support for a specific period of time in early recovery. The structure of residential treatment allows positive changes and stabilization in patients' attitudes and lifestyles. The duration of residential treatment varies. Some treatment may be as short as 30 days, whereas other treatment may last up to 1 year.

TCs, a common type of long-term residential treatment, typically use group activities directed toward effecting significant changes in the residents' lifestyles, attitudes, and values. They emphasize prosocial behavior and strengths-based strategies for improved decision making (NIDA, 2015). Many referrals to TCs take place through the court system. In fact, TCs were originally

designed for patients with heroin use disorder, low socioeconomic backgrounds, and long-term histories of criminal involvement.

Halfway Houses

Halfway houses (also known as sober living environments or facilities) provide transitional support for people who have completed residential treatment and are still attending formal treatment, like outpatient care (Polcin et al., 2010), but would benefit more from increased structure or support than from solitary community living. Halfway-house program requirements usually include specified community involvement (e.g., employment or enrollment in school), and abstinence from mood-altering substances. Evening group activities are structured around residents' work schedules. Programs generally require out-of-pocket expenses and have limited insurance coverage or reimbursement.

PATIENT PLACEMENT: AVOIDING THE COOKIE-CUTTER APPROACH

Long-term residential treatment can be enormously helpful for many patients. But not all people with stimulant use disorders need this level of care right away or even ever. A one-size-fits-all approach to choosing a treatment setting—such as sending everyone to residential treatment for 60 days—should not be used. Rather, clinicians should consider each patient's needs, preferences, and life circumstances individually. Using patient placement criteria, such as those from ASAM, or clinical assessment can help clinicians and patients make informed, tailored decisions.

Clinical Issues To Consider

Clinicians should be prepared to take into account a number of clinical challenges when doing treatment planning with patients. Exhibit 4.1 summarizes the most common clinical issues encountered and strategies to manage them (Rawson et al., 2021).

EXHIBIT 4.1. Stimulant Use: Managing Common Clinical Issues

Issue	Clinical Consideration	Management Strategy
Secondary substance use	<p>An individual may use multiple substances to enhance the physical or psychological effects of each drug, to counteract the effects of one or more drugs, to prolong a drug's effects, or to experience a new effect.</p> <p>One who uses stimulants often also uses:</p> <ul style="list-style-type: none"> • Alcohol. • Opioids (e.g., heroin, fentanyl, prescription opioids). • Benzodiazepines. • Cannabis. 	<ul style="list-style-type: none"> • Assess individuals using opioids for opioid use disorder (OUD) and treat with medications for OUD.* • Assess individuals using alcohol for alcohol use disorder (AUD) and treatment with AUD medications, including naltrexone.* • Assess individuals using benzodiazepines for dependence, and, if needed, provide medical withdrawal assistance. • Offer motivational interviewing (MI) and other evidence-based behavioral strategies.
Overdose risk	<p>Much of the cocaine and methamphetamine (MA) that is now available contains fentanyl and heroin.</p> <p>Individuals using stimulants that include fentanyl have an increased risk for overdose.</p> <p>Current supply of MA is very potent and can create MA overdose, including seizure, stroke, very high temperature, and heart attack.</p>	<ul style="list-style-type: none"> • Assess patient awareness of dangers from fentanyl and educate about risks. • Encourage patients to use fentanyl test strips to determine whether stimulants have been mixed or cut with fentanyl. • Train staff, patients, and family members on naloxone use and make naloxone available to patients, their families, and the community. • Monitor patients closely for opioid overdose symptoms from fentanyl (or heroin) mixed with MA or cocaine. • Train staff in use of MA overdose strategies, including how to address stroke and hyperthermia.
Intoxication	<p>Stimulants cause:</p> <ul style="list-style-type: none"> • Euphoria. • Hyperexcitability. • Hypersexuality. • Increased locomotor activity. • Agitation. • Psychotic symptoms, including paranoia and hallucinations. • Dilated pupils (National Institute on Drug Abuse, 2021b; Yasaei & Saadabadi, 2021). 	<ul style="list-style-type: none"> • Try to calm the patient down (i.e., create a soothing environment). • Consider pharmacologic treatment (e.g., benzodiazepines, antipsychotics) for patients who exhibit severe symptoms of intoxication. • Note: No medications are currently available to reverse MA overdose. • Note: Cocaine intoxication typically lasts 2–4 hours, whereas MA intoxication can last 12 hours or more.
Co-occurring mental and stimulant use disorders	<p>One of the challenges clinicians face is making a distinction between independent psychiatric disorders, psychiatric disorders as a result of the stimulant use, and psychiatric symptoms that arise from intoxication and withdrawal.</p>	<ul style="list-style-type: none"> • Consider integrated treatment options, regardless of the underlying cause of the co-occurring diagnosis. • Lack of adequate treatment for either disorder may interfere with overall recovery; coordinate services between SUD clinicians and mental health service providers if SUD treatment staff do not treat mental disorders.

Continued on next page



EXHIBIT 4.1. Stimulant Use: Managing Common Clinical Issues

Issue	Clinical Consideration	Management Strategy
Psychosis	Stimulant use can cause psychotic symptoms (e.g., auditory and visual hallucinations, paranoia). Mania also may occur. Stimulant-induced psychosis is generally transient; but persistent MA psychosis can resemble psychosis in schizophrenia.	<ul style="list-style-type: none"> Consider an antipsychotic medication to address acute symptoms. Consider continuation of antipsychotic medications for long-term management of persistent psychosis.
Violence	MA use increases the risk of violent behavior (McKetin et al., 2014).	<ul style="list-style-type: none"> Understand the relationship between stimulant use and violence, and be aware of the consequences of violence for individuals using stimulants, their families, facility staff, and other patients.
Cognitive deficits	Stimulant misuse leads to attention and memory problems that can interfere with an individual's ability to engage in treatment approaches that involve learning. Stimulant misuse can also lead to executive dysfunction, including difficulties with problem-solving, planning and organization, and reasoning (C. Ellis et al., 2016; Wilens et al., 2017).	<ul style="list-style-type: none"> Inform patients about cognitive deficits and use strategies that provide repetition of information and do not depend on optimal memory. Reserve treatments that require more complex cognitive functioning until a patient's cognition is restored after a period of abstinence from stimulants. Assess for cognitive deficits and teach staff to be aware of any deficits.
Stimulant withdrawal	Stimulant withdrawal symptoms comprise severe fatigue, cognitive impairment, feelings of depression and anxiety, anergia (lack of energy), confusion, and paranoia. Most patients experiencing acute withdrawal/early-phase abstinence will have most of their symptoms resolve in 2–10 days.	<ul style="list-style-type: none"> Suggest that patients rest, exercise, and eat a healthy diet, which is the best management approach for most people in withdrawal. Patients with heightened agitation and sleep disturbance may respond to pharmacotherapy, but acute depression and anhedonia associated with early abstinence generally resolve without intervention. Be aware of possible dehydration and hyperthermia.
	Individuals may experience cravings associated with specific cues, such as objects (e.g., cash), people (e.g., relatives who use drugs), other substances (e.g., cannabis), places (e.g., areas where stimulants are sold or used), time periods (e.g., weekends, evenings), and emotional states (e.g., depression, boredom; A. R. Childress et al., 1999).	<ul style="list-style-type: none"> Educate patients in treatment about the powerful impact of cue-induced cravings, and help them identify strategies to avoid situations in which there are “triggers.”
	Once acute withdrawal subsides and the person starts to feel better, they may experience hypersexuality and impaired sexual functioning, leading to mental distress (Rawson et al., 2002).	<ul style="list-style-type: none"> Educate patients about the possibility of changes in sexual function during later phases of recovery.

Continued on next page

EXHIBIT 4.1. Stimulant Use: Managing Common Clinical Issues

Issue	Clinical Consideration	Management Strategy
Severity of disorder and level of care	Patients may receive treatment services at various levels within the continuum of care. Levels range from prevention and early intervention to inpatient and residential services. Assessing the required level of care for each patient based on the severity of the patient's disorder is critical. Patient placement criteria, such as the American Society for Addiction Medicine's, can be used to match severity to level of care needed.	<ul style="list-style-type: none"> • Ensuring access to care is a primary consideration given the potential for overdose. Evaluate the patient's needs and try to match services at the appropriate level, and then step up to more intense treatment or down to less intense treatment as needed. • Engage peer recovery support specialists or case managers who can be helpful in continuing care, removing obstacles to recovery, and linking patients to specialty treatment. • Based on the risk of overdose, ensure availability of treatment and retention in treatment as primary goals for all programs working with people actively using stimulants. • Consider the presence of psychosocial stressors that may affect level of care needed, such as involvement in the criminal justice system or a lack of housing.

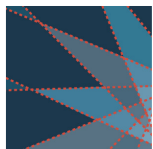
* Because naltrexone is an opioid antagonist, patients who take opioids and are prescribed naltrexone for AUD or OUD must abstain from opioids for 7 to 14 days (depending on type of opioid) before starting naltrexone treatment. The purpose of this waiting period is to avoid precipitating opioid withdrawal (Substance Abuse and Mental Health Services Administration, 2020h, 2020o).

Engaging and treating people who are actively using stimulants, in withdrawal, or in early recovery is challenging. Understanding the experience of the patients in conjunction with clinical concerns is essential for planning and implementing therapy practices to meet patient needs and preferences. Again, when working with these patients, keep in mind that the psychosocial approach with the most research support is CM, with CBT/RP, community reinforcement, and MI also being well-supported interventions. Moreover, mutual-help programs, such as Crystal Meth Anonymous and Narcotics Anonymous, can help individuals with stimulant use disorders manage relapses and enhance recovery.

Summary

Several empirically tested nonpharmacologic treatments for stimulant use disorders are available, with CM having the strongest weight of evidence. CBT/RP, community reinforcement, and MI also have good though less robust data to support their use to treat stimulant use disorders. Less rigorously studied yet still appropriate approaches, such as mindfulness meditation and prescribed physical activity, can also be used to supplement SUD care and potentially help patients improve abstinence and other health outcomes. Clinicians have a wide range of options to help patients with stimulant use disorders reduce or stop their substance use, improve their health, regain functioning (e.g., obtain or return to work), and achieve long-term recovery.

This page intentionally left blank.



Chapter 5—Practical Application of Treatment Strategies

KEY MESSAGES

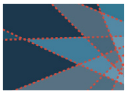
- Clinicians may begin engaging patients who use stimulants before these patients have any motivation to change their pattern of use. Clinicians should use motivational interviewing techniques to assess patients' stage of change, ambivalence to change, and motivators for change as part of the initial assessment for treatment.
- Strategies that clinicians can use to maximize patient engagement include discussing treatment expectations, offering multiple treatment options, using a person-centered and respectful approach, conveying empathy and concern, identifying barriers to treatment engagement or participation that would affect success, and working collaboratively with patients to develop a clear treatment plan and framework that can be changed as necessary.
- Clinicians should initiate treatment of new patients by working with them to set treatment goals, discussing reducing or discontinuing all substance use, fully assessing their clinical needs, and helping them manage stimulant withdrawal. Clinicians should then focus on helping these patients progress through the continuum of substance use disorder care.
- Clinicians can use several strategies to help patients maintain progress in recovery, such as teaching functional analysis of stimulant use; reinforcing positive behaviors with incentives (i.e., contingency management); offering relapse prevention tools; teaching ways to avoid high-risk situations; providing social skills training; linking patients to vocational counseling; and promoting connections to family, friends, and the community.

The Food and Drug Administration (FDA) has not—as of the publication date of this document—approved any medications for the treatment of individuals with stimulant use disorders. Therefore, Chapter 5 focuses on applying behavioral and psychosocial approaches to improving treatment outcomes for individuals with stimulant use disorders. Consensus panel recommendations for the Substance Abuse and Mental Health Services Administration's (SAMHSA) original Treatment Improvement Protocol (TIP), which were augmented by field review feedback, have been reviewed and updated. Whenever possible, the chapter presents treatment strategies that are supported by empirical evidence. However, because many stimulant use treatment issues have not been systematically researched, current clinical practice is also discussed.

Individuals seeking help for stimulant use disorders can receive their treatment in a variety of settings. The strategies described in this chapter emphasize techniques used in outpatient substance use disorder (SUD) care. However, many, if not most, of these strategies and techniques can be integrated into other treatment settings across the continuum of care.

This chapter describes the key aspects of stimulant use disorders in the order in which they typically unfold to provide clinicians with a roadmap for systematically addressing clinical issues as they emerge.

This chapter assumes that structured outpatient treatment will be viewed as one interdependent component of a larger SUD treatment process and system. Many people with stimulant use disorders can experience the following:



- Medical problems or emergencies
- Psychiatric problems or crises
- Social, legal, or employment problems

Therefore, this chapter, while focusing on outpatient treatment of stimulant use disorders, acknowledges the critical importance of various settings and processes along the continuum of care.

LEVELS OF CARE AND STIMULANT USE DISORDER TREATMENT

Chapter 3 describes the medical and mental health factors to consider to ensure the safe admission of patients into care settings. The American Society of Addiction Medicine (ASAM) Criteria establishes comprehensive guidelines to ensure that patients with SUDs enter treatment at the appropriate level of care, remain in care for the necessary duration, and are transferred to another level of care when they are ready. ASAM Criteria assesses six dimensions for individuals:

1. Acute intoxication and/or withdrawal potential
2. Biomedical conditions and complications
3. Emotional, behavioral, or cognitive conditions and complications
4. Readiness to change
5. Recurrent or continued use or continued risk potential
6. Recovery and living environment

Clinicians can use ASAM Criteria to prioritize patients' treatment needs and to identify the areas where patients are most likely to have a successful response to treatment (SAMHSA, 2021c). Clinicians can also reference state-specific placement criteria that satisfy requirements outlined in state statutes for SUD admissions (if available).

Source: Mee-Lee D, Shulman GD, Fishman MJ, Gastfriend DR, Miller MM, eds. The ASAM Criteria: Treatment Criteria for Addictive, Substance-Related, and Co-Occurring Conditions. 3rd ed. Carson City, NV: The Change Companies®; 2013.

People With Stimulant Use Disorders Seeking Treatment

To effectively meet the needs of people using stimulants, healthcare staff throughout the continuum of care must understand patients' unique perspectives. For example, individuals with opioid use disorder (OUD) may initiate contact with the treatment system when they are experiencing opioid withdrawal. Taking FDA-approved medications for OUD that alleviate opioid withdrawal symptoms may be patients' first foray into formal SUD treatment. SUD care settings that can provide both OUD medication and behavioral support are better equipped to engage and retain patients in care.

People with stimulant use disorders may approach the treatment system with a different set of priorities than do people with OUD. Although the priorities of people with stimulant use disorders and the assistance they seek vary, they often share several common pretreatment perspectives.

"Bad Things Are Happening"

Admission interviews with people who use stimulants may reveal that they are seeking treatment mainly because this use has resulted in negative consequences, such as legal, job-related, medical, family/relationship, financial, and psychiatric problems (Herbeck et al., 2014; Pedrelli et al., 2015; Vayalapalli et al., 2011). Initially, these individuals may focus on receiving assistance to address these negative consequences rather than on reducing their stimulant use. This attitude is consistent with Maslow's Hierarchy of Needs (Maslow, 1943), which states that individuals must meet their most basic needs (i.e., physiologic and safety needs) before they can pursue higher level needs (i.e., needs related to love and belonging, self-esteem, and self-actualization). By understanding patients' motivations for seeking treatment, clinicians can better meet patients "where they're at."

“Life Is Out of Control”

Patients engaging in treatment for stimulant use disorder may say, “My life is out of control.” They point to their excessive behaviors associated with obtaining, using, and recovering from using cocaine or methamphetamine (MA). These behaviors can lead to:

- Financial instability and/or illegal activities (Cheng et al., 2010; Gizzi & Gerkin, 2010; Maiorana et al., 2021).
- Lack of routine self-care (Nassar & Ouanounou, 2020; Yasaei & Saadabadi, 2020); examples include insufficient eating, sleeping, bathing, and oral hygiene.
- Diverse or personally atypical sexual activities (Maiorana et al., 2021).
- Strained familial and spousal relationships (Abdul-Khabir et al., 2014; Cheng et al., 2010) resulting from, for example, spending subsistence money on drugs, failing to care for children, or engaging in marital infidelity.
- Homelessness (McKenna, 2013; Walls & Bell, 2011); examples include staying on a friend’s couch, staying in a car, and renting by the week at a motel.

Emotional turmoil accompanies these developments, including (Ciccarone, 2011; J. C. Maxwell, 2014):

- Cycles of euphoria and depression and heightened emotional lability.
- Intense anxiety, fear, guilt, and shame over medical, financial, legal, and personal relationships. Patients can also experience these feelings when they are unable to determine whether recent behaviors or events that took place during a period of psychosis were real or imagined.
- Anergia (lack of energy) and anhedonia (inability to feel pleasure) during periods of abstinence.
- Anger, paranoia, and irritability during periods of use or abstinence.

Patients who are in emotional turmoil may present with tangential (off-topic) or pressured speech or with slowed speech.

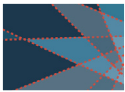
Cognitive Impairment/Clinically Significant Paranoia

Chapter 3 documents that the use of stimulants may produce significant cognitive impairment (Lappin & Sara, 2019; J. J. Mahoney, 2019; Wunderli et al., 2016) and may be accompanied by severe paranoia. Individuals have expressed concentration difficulties, impaired short-term memory, and a relatively short attention span. Patients using stimulants may also experience paranoia and altered persecutory perceptions of reality. To overcome these effects, clinicians must create a safe environment and gain patients’ trust while collaborating with them to establish a treatment plan and treatment goals.

Ambivalence to Change/Skepticism About Treatment

Clinicians new to working with individuals with stimulant use disorders may be frustrated and angered by what they perceive as their patients’ “lack of motivation” or “denial.” Ambivalence is part of the recovery process and is often associated with behavioral changes that lead to improved health outcomes. Clinicians need to remember that individuals receive some benefit from using stimulants. Addressing positive aspects of stimulant use allows for an open discussion about the negative consequences and motivations for change. Motivational interviewing (MI) can help clinicians understand and navigate patients’ ambivalence to change. For example, clinicians can ask questions such as “What is good about using stimulants?” and “What is not so good about using stimulants?” These questions can enhance engagement and prompt conversations about the reasons for behavior change.

In addition, stimulant use is a byproduct not only of the neurobiology of craving, but also of dysregulated reward systems (see Chapter 2 for discussion).



Craving

The experience of craving a substance characterizes almost all SUDs. However, the craving for stimulants may be more intense than any other cravings patients have experienced. Chapter 2 describes research on the neurophysiologic correlates of stimulant craving. People who use stimulants have likely experienced craving but may have little understanding of the biologic underpinnings of this experience.

The power and intensity of this craving response can make it exceptionally difficult for people with stimulant use disorders to interrupt their pattern of use (Sinha, 2013), especially early in treatment. (This is especially true for those who use the rapid-delivery routes of smoking or injection.) Some people cannot imagine how counseling or other forms of nonresidential treatment can help with this overwhelming sensation.

Other Challenges Frequently Encountered in Treatment

Clinicians treating patients with stimulant use disorders may also encounter:

- Dysphoria (sad mood) that occurs upon discontinuing stimulant use (MacLean & Sofuoglu, 2018).
- Compulsive sexual behavior (especially for those who use MA), which is often reported to be at least as difficult to control as the stimulant use (Berry et al., 2020; Loza et al., 2020).
- Discouragement given previous attempts in and outside of treatment to end stimulant use, only to experience return to even more severe levels of use.
- Mental disorders that co-occur with or are induced by stimulant use disorders. (See the discussion on assessing for co-occurring mental disorders in this chapter's "Complete Assessment of Clinical Needs" section and the Chapter 6 section "Individuals With Co-Occurring Mental Disorders.")

These issues may interact in various ways and affect individuals in different ways, resulting in treatment experiences that are unique to individual patients.

Treatment Needs of People With Cocaine Use Versus Methamphetamine Use Versus Prescription Stimulant Misuse

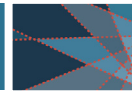
Limited empirical evidence exists for designating any one psychosocial approach as being differentially effective for these three stimulant groups: cocaine, MA, and prescription stimulants. Therefore, the treatment recommendations made in this chapter apply to people using cocaine and MA and misusing prescription stimulants. Regardless of the type of stimulant, care must be coordinated.

Maximizing Treatment Engagement

Make Treatment Accessible and Support Continued Participation

Treatment services need to be highly accessible, because people with stimulant use disorders are seen in a broad range of settings. Research suggests that numerous factors can hinder access to SUD treatment, including provider-related factors, such as shortages of SUD treatment workers and stigmatizing attitudes they may have about SUDs; market and environmental factors, like Medicare and Medicaid reimbursement issues; and insurance factors, like the availability of in-network clinicians in a geographic location (O'Brien et al., 2019). Several factors are vital to treatment engagement:

- **Accommodating patients' schedules.** Access to care is improved when treatment is provided during hours and days that are convenient for patients (i.e., not just during traditional 9 a.m. to 5 p.m. business hours). Daytime treatment programming may be helpful for patients who do not work and find boredom and lack of daytime activities significant contributors to substance use. Patients who work during the day may need to attend evening or weekend treatment sessions. Having a flexible treatment schedule allows clinicians to emphasize employment and other household responsibilities as protective factors in recovery.



WHY COORDINATED CARE IS SO CRITICAL

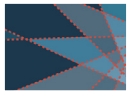
Coordinated care encourages members of the treatment team to work collaboratively and in a person-centered manner. Treatment occurs along a continuum that combines medical care with psychological and social interventions. Clinicians collaborate on treatment activities, which are tailored to each patient's needs. To facilitate coordinated care, clinicians should obtain a signed release form for all of the patient's care providers during the initial assessment. The patient may exit treatment quickly, so having a signed release form allows the treatment team to coordinate with other providers to help the patient reengage in treatment.

People with SUDs typically have numerous health- and behavioral health-related issues that interact with one another (Radfar & Rawson, 2014). Clinicians cannot effectively address SUDs using a fragmented approach that ignores other problems their patients are coping with and may or may not be receiving services to address. This interaction is why coordinated care is so critical to ensuring successful SUD treatment outcomes for patients.

Coordinated care models emphasize the engagement of multidisciplinary staff to fully address patients' physical and mental health needs through open communication, shared knowledge and decision making, individualized treatment plans, and the use of evidence-based best practices. For instance, a woman in treatment for cocaine use disorder might benefit from seeing a drug and alcohol counselor to help her with recovery and abstinence, a primary care provider to help monitor for any medical complications or conditions (e.g., those that accompany stimulant withdrawal), a psychologist or licensed professional counselor to help her better manage longstanding trauma symptoms and recent depressed mood, a psychiatrist to monitor her antidepressant medication, a social worker to assist in navigating access to public assistance programs (e.g., Temporary Assistance for Needy Families), a peer recovery support specialist to share common experiences and to serve as a mentor, and a case manager to help coordinate care.

Coordinated care ensures that all members of the care team are equipped with accurate, current information about a patient's diagnosis, history, treatments, and treatment goals. They work collaboratively to achieve those goals effectively, in a timely manner, and without redundancies. Coordinated care models have been scrutinized in research and deemed effective in the treatment of SUDs, particularly in primary care practices (LaBelle et al., 2016; Lagisetty et al., 2017; Pew Charitable Trusts, 2020).

- **Addressing concrete needs.** Research has demonstrated the importance of addressing patients' concrete needs, including transportation, housing, and finances (Browne et al., 2016; Priester et al., 2016). Clinicians may need to establish protocols for rapidly addressing transportation barriers (e.g., by providing bus fare cards or cab/rideshare fare, using vans to drive patients to and from their appointments). Locating SUD care settings near public transportation and in areas viewed as safe for evening visits improves accessibility for patients. Individuals with disabilities may need special accommodations (e.g., wheelchair access ramps, electronic doors, elevators, assistive communication devices). Clinicians and organizations can seek philanthropic funds as well as federal and state grants to assist with addressing these particular needs.
- **Providing onsite services.** Some logistical barriers can be overcome by providing onsite services, through agreements with subcontractors, or by referrals. These services can include providing onsite childcare, referrals to temporary shelters, vouchers for lunches, targeted financial assistance, and help with insurance paperwork or filing for disability. "Warm handoff" referrals where treatment staff personally contact personnel from other settings facilitate a successful referral process.
- **Reaching underserved populations.** In rural areas, small satellite sites may be needed to bring treatment closer to patients (e.g., using



space in primary care clinics or social service agencies). SUD care services should also offer telehealth technology—in place of or in addition to face-to-face treatment—for people with mobility or distance barriers.

Respond Quickly and Positively to Initial Inquiries

People who use stimulants may make their first contact with the SUD treatment system by telephone, through email, or via online contact (e.g., the treatment center’s website, social media). They may drop by a clinician’s office, an SUD care facility, or a campus health center. Some may make initial contact with treatment when they check in with their probation/parole officer or engage with justice-involved staff. The manner in which the receptionist, intake worker, clinician, or other staff person handles the initial contact may affect whether the individual decides to enter treatment. Methods that promote successful treatment engagement include:

- Answering telephone or online inquiries immediately for as many hours per day as possible (e.g., not placing people on hold, not requiring callbacks).
- Using 24-hour hotlines to facilitate late-night and weekend inquiries.
- Monitoring websites (including chat features) and social media accounts for new messages daily.

Seeking SUD care can be a difficult and painful process. Access to care improves when there is maximum flexibility in responding to all kinds of treatment inquiries.

Schedule Initial Appointments With Minimal Delay

An individual’s decision to seek help may last for only a brief period, so the initial interview should take place as soon as possible after first contact. SUD treatment providers may not always have the resources to conduct thorough intake interviews immediately, and these interviews may not always be feasible (i.e., if the patient is in crisis and needs immediate intervention services for stabilization).

If possible, interim services should be provided until a more thorough intake can be completed, including any organization- or state-mandated health screenings. For example, a brief trauma-informed interview or a partial intake session within 24 hours of contact might identify acute needs that require immediate attention. SUD treatment providers can also hold orientation meetings in lieu of placing names on waiting lists. The use of telehealth can help clinicians stay connected to patients who are waiting for admission to higher levels of care. If a waiting list cannot be avoided, staff members can draw on the patient’s treatment readiness by telephoning to express concern about the patient’s well-being, conducting mini-assessments, providing basic recommendations (e.g., attending a mutual-help group meeting), connecting patients to peer recovery support specialists, and working with the patient to locate other available treatment options within the same level of care. These efforts serve as a temporary bridge between the initial contact and a thorough interview and assessment.

Assessment Procedures To Enhance Treatment Engagement

Use Brief Screening Tools

Initial screenings that are brief, focused, and nonrepetitive enhance engagement. Free tools are available for clinicians to screen for SUDs, including stimulant use disorder and common co-occurring disorders, like alcohol use disorder and OUD. For example, clinicians can use the National Institute on Drug Abuse (NIDA) Quick Screen V1.0 to screen patients age 18 or older for general substance misuse. The NIDA-Modified Alcohol, Smoking and Substance Involvement Screening Test (NIDA-Modified ASSIST) V2.0 provides clinicians with additional questions to ask about recent and lifetime use of specific substances. (For both tools, see <https://www.drugabuse.gov/sites/default/files/pdf/nmassist.pdf>.)

Identify Patients’ Expectations and Provide a Service Orientation

Identifying patients’ expectations—as well as their fears, concerns, and anxieties—is important.

For example, patients with previous treatment experiences may have anxieties about treatment failure or trauma associated with treatment. Clinicians should work to address patients' worries through information and education about SUD care and the treatment process. This information can help decrease or eliminate fear of the unknown and create a safe space. A thorough, clear, and realistic orientation about stimulant use disorder treatment focuses on:

- Basic treatment components and processes, including length of treatment and continuing care/recovery planning.
- Rules of the SUD treatment provider.
- The SUD treatment provider's expectations about participation, such as the amount of time that is required and what happens at each phase.
- The patient's expectations of what the SUD services can do.
- Completion criteria.
- Expectations and possible treatment or care plan revisions if the patient continues to struggle with substance use.

Clinicians may need to repeat this information, because patients with cognitive deficits secondary to prolonged stimulant use may have difficulty with memory or trouble following long and complex instructions and explanations. Clinicians can address this issue with simple and clear introductory information and instructions. Patients with and without cognitive deficits can benefit from also receiving brief handouts with this information written at an appropriate reading level.

Offer Options

Motivation research demonstrates strongly and consistently that people are most likely to engage in an action when they perceive that they have personally chosen to do so. To perceive that one has a choice, alternatives must be available from which to choose (Köpetz et al., 2013; Miller, 1985).

A flexible, trauma-informed, recovery-oriented approach to treating individuals with SUDs includes, where appropriate, seeking patient input into the type of treatment initiated and the

treatment setting (World Health Organization [WHO] & United Nations Office on Drugs and Crime [UNODC], 2020). This ethical, best practices approach to SUD treatment respects patients' autonomy (WHO & UNODC, 2020), provides them with options, and encourages their collaboration on the treatment approaches and strategies that are the most acceptable to and promising for them.

Involve Significant Others

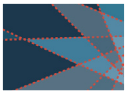
Whenever possible, clinicians should involve family members and significant others who support the goals of the treatment process—including the initial assessment and intake processes—provided patients give written consent for their inclusion. Patients who do not have close family relationships may wish to involve close friends whom they consider family. Significant others benefit from receiving information about the development of SUDs, SUD care, assessment results, troubleshooting concerns for continued use, and the next steps for themselves and their loved one.

In the SUD care setting, clinicians can work with significant others to help them better understand their role in the SUD treatment process and their possibly complicated relationship with the person in treatment. Information on mutual-help groups for significant others, such as Nar-Anon and Al-Anon, should also be provided.

Staff Skills To Enhance Treatment Engagement

Several basic therapeutic skills can enhance treatment engagement in people with stimulant use disorders:

- **Treating patients respectfully and calmly.** Patients with stimulant use disorders may be frightened, disoriented, and cognitively impaired. Clinical and nonclinical staff members can alleviate fears about entering treatment by offering positive feedback, answering questions honestly, and letting patients know that staff members want to help them. When people with stimulant use disorders are treated calmly and respectfully, trauma responses and protective behaviors are rare.



- **Conveying empathic concern.** Clinicians who provide advice and recommendations in a friendly, engaging, empathic, straightforward, and nonjudgmental way can calm patients and increase the likelihood for positive treatment outcomes (Elliott et al., 2018).
- **Refraining from fighting resistance.** Fighting resistance to change or treatment is counterproductive and can harm the therapeutic alliance. Patient-centered, nonjudgmental, and nonconfrontational approaches are effective at improving outcomes in people with SUDs (Blonigen et al., 2015), including stimulant use disorders.

ADDRESSING PATIENT AMBIVALENCE ABOUT REDUCING SUBSTANCE MISUSE BEHAVIORS

People with SUDs may feel ambivalent about entering treatment or becoming abstinent, especially during the early stages of recovery (SAMHSA, 2019). Clinicians can use MI techniques to help patients with SUDs understand stages of change and resolve ambivalence toward behavior change by helping them directly confront and acknowledge their hesitation, while highlighting motivations or reasons to change (Lindson et al., 2019; Searight, 2018). Harm reduction techniques should be introduced to people who are not ready to enter formal treatment, to minimize risks associated with continued misuse of stimulants and other substances. (See the Chapter 4 text box “The Importance of Teaching Harm Reduction.”)

Treatment

Treatment for individuals with stimulant use disorders involves procedures that address a series of clinical issues in a fairly predictable sequence. To organize treatment strategies, it can be helpful to view the treatment process as consisting of engagement, initiation, stabilization, and maintenance with a long-term support plan. These are not discrete or sequential phases of treatment; in some instances, they occur simultaneously or in a different order. For example, some patients

engage in treatment and initiate abstinence at the same time; others may need to be stabilized prior to treatment initiation.

At the beginning of treatment, patients may feel overwhelmed and may struggle with motivation in the context of cravings and triggers. Treatment plans must give patients a clear framework for their treatment experience. This framework sets up specific expectations and provides patients with the benchmarks they need to plan their treatment participation and measure their progress. Treatment plans should include SMART goals: Specific, Measurable, Achievable, Relevant, and Time Bound. Setting SMART goals at the beginning of treatment can help patients achieve small gains toward recovery and keep them motivated to engage in further treatment.

Strategies for Engagement

Stimulant use withdrawal symptoms, specifically fatigue, dysphoric mood, and lack of motivation, may make initial engagement with SUD treatment clinicians difficult. Some patients continue to use stimulants initially. For this reason, the goal of patient interaction in this first phase may strictly be for the patient and clinician to initiate a therapeutic relationship that engages the patient in services.

Clinicians can reference level-of-care tools such as the American Society of Addiction Medicine (ASAM) Criteria to determine the appropriate level and duration of care for individuals with stimulant use disorders who are entering treatment. The ASAM Criteria provides guidance about multidimensional assessment and recommendations for placement in the continuum of care.

Several immediate priorities can encourage treatment engagement in the first weeks of treatment:

- Establish treatment attendance.
- Discontinue or reduce use of stimulants and secondary substances of misuse.
- Complete assessment of clinical needs.
- Resolve immediate crises.

Establish Treatment Attendance

Initiating a routine of treatment attendance involves giving patients:

- A clear expectation of when and where they should be attending treatment.
- A detailed explanation of what happens during treatment sessions.
- Reinforcement when they attend treatment on schedule.
- Reminders when they miss treatment.
- Guidance, if they need it, on how they will travel to treatment sessions.

During the initial weeks, patients may be early or late for their scheduled appointments or may show up under the influence. They may frequently be in crisis or a state of confusion. Patients may come to the treatment setting only when it is convenient. Some patients may need a higher level of care or another assessment. However, patients should rarely, if ever, be discharged from services under these circumstances.

Engagement with SUD care offers clinicians an opportunity to develop a trusting relationship with patients and to encourage appropriate behavior by reinforcing the importance of attendance. Engagement at this time is critically important because of the high dropout rates of this patient population at the start of treatment. Clinicians should highlight successes when patients attend treatment and celebrate those who reengage in treatment after taking a break from it.

Patients with stimulant use disorders need to hear that they should participate in and return to SUD care, even if they are using stimulants or other substances. Participation is enhanced with reminder cards, flyers, and schedules with the message that patients are expected to return for their appointments and that they will always be welcomed back. Agencies should have a policy regarding patients attending treatment while using substances. Clinicians need to communicate with patients about this policy.

Use incentives to reinforce treatment participation

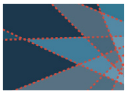
A powerful strategy for increasing treatment involvement and establishing treatment engagement is to provide immediate positive consequences for desired behaviors to incentivize progress in treatment (Kirby et al., 2013). These incentives will differ among patient populations.

Some patients prefer gift cards for retail items or meal coupons; others appreciate clothes for themselves or their children or rebates for payments. Some SUD treatment providers hold brief graduation ceremonies or present certificates of completion. Kirby and colleagues (2013) demonstrated the effectiveness of incentives for substance-free urinalyses through the use of vouchers that could be traded for prizes (e.g., gift certificates). Research has shown that contingency management (CM) approaches demonstrate improved treatment attendance and retention (McDonell et al., 2013). Establishing what the incentives are, how they are obtained, and how the tasks associated with the incentives are verified should be discussed and provided in writing for patients to review.

See the “Contingency Management” section in Chapter 4 for more information.

Reach out to no-shows

Staff members should contact patients who fail to show up for scheduled visits to encourage their participation and inquire about possible crises that prevent them from fully engaging. Staff can send a letter, write an email, or phone or text patients to remind them that their participation is missed. This is also an opportunity to partner with peer recovery support specialists. Having peer recovery support specialists initiate contact with patients after no-shows can feel less threatening, and the patients may be more responsive. Policies and procedures for reaching out to no-shows should also be developed. Such policies and procedures need to conform to all applicable confidentiality requirements.



Create a positive environment

Research demonstrates that positive environments—ones that promote growth and well-being—improve mental health and social functioning (Corral-Verdugo & Frias-Armenta, 2016). Patients with stimulant use disorders may feel that they do not belong in treatment because they:

- Do not see themselves as having a disorder.
- Do not like the physical SUD care setting or location.
- Perceive that they do not need SUD care to address their stimulant use.
- Think they cannot relate to other patients.
- Think that prescription stimulant misuse isn't as serious or dangerous as using illicit substances.

Rather than attribute these beliefs to defense mechanisms, SUD care workers should take steps to improve patients' comfort level and experiences with the service. Administrative staff who answer the phone or greet patients at the front desk can set the tone by being welcoming.

Clinicians should work to create a trauma-informed safe environment for all patients. For example, SUD treatment providers can establish connections between new patients and peer recovery support specialists who are trained to dispel fears and concerns about SUD care and the treatment process. Peer recovery support specialists can use their lived experiences to help patients who have recently initiated treatment relate to patients who are already established in treatment.

Discontinue or Reduce Use of Stimulants and Secondary Substances of Misuse

Encourage abstinence or reductions in use immediately

After an initial assessment interview, clinicians should ask patients to agree to a trial period of abstinence or, if abstinence is not possible, reductions in substance misuse. The first interview can end with a specific plan for making these changes, such as abstaining from or reducing substance misuse until the next SUD care visit. Strategies to help patients initiate abstinence or reductions in substance misuse include preparatory

group therapy that involves motivational enhancement techniques (Miller & Rollnick, 1991). These therapy sessions are brief but frequent (e.g., three to five times per week) and can include urine testing.

Individuals may be at a different stage of readiness for change (Prochaska et al., 1992) for each substance they use. For example, they may have decided to stop using stimulants but are still contemplating whether to stop drinking alcohol. Using MI strategies in individual and group therapy settings may move such patients from the contemplation phase to decision and action phases with regard to alcohol use.

Establish a daily schedule

Planning and scheduling are important ways to deter individuals with stimulant use disorder from spending a lot of time alone or having big blocks of time without planned activities. Typically, the daily routine of individuals with stimulant use disorders revolves around seeking, using, and recovering from the effects of stimulants. To break this pattern, patients are taught to use daily schedules to structure their lives and to help them monitor their actions. Using schedules is particularly critical during treatment initiation and stabilization. Clinicians can work with their patients to create simple daily and weekly schedules. Schedules should include time for:

- SUD care visits.
- Mutual-help meetings (e.g., 12-Step meetings, Self-Management and Recovery Training [SMART Recovery] meetings).
- Healthy meals.
- Healthy social activities.
- Exercise, recreation, and leisure.
- Medical and mental health appointments.

Initiate a urinalysis schedule

Establishing a regular urine drug screening protocol with patients at the onset of treatment helps alleviate fears about surveillance. There is a difference between supportive and surveillance urine toxicology screenings: Supportive urine toxicology screening can be a useful tool to assess the treatment plan and determine whether treatment is working. When discussing urine

toxicology results, the clinician should emphasize that the results reflect the effectiveness of treatment and are not meant to identify patient failures. The clinician should use nonjudgmental language, such as “The results indicate a return to use,” and avoid value-laden terms like “clean” and “dirty.”

Typically, urine toxicology testing tapers as treatment progresses, patients stabilize, and the clinical relevance of the tests become less important. Tests are spaced to ensure that results from the previous test are available before the next test is conducted and to avoid exceeding the sensitivity limits of standard laboratory testing methods, which generally means spacing tests no more frequently than every 3 days. More frequent testing generally provides little information of clinical relevance. However, if the patient appears intoxicated or has admitted to misusing substances, testing may need to be repeated to establish a baseline. SUD treatment providers also conduct random testing, although it is advisable to test on days that closely follow periods of high risk, such as holidays, paydays, and weekends.

Urine collection should be conducted in a trauma-informed way. Strategies for this process include the following:

- Provide patients with information about the urine collection process so they know what to expect (Scoglio et al., 2020).
- Allow patients to voice concerns about the urine collection process, and respond in an empathic manner (Scoglio et al., 2020).
- Acknowledge that the urine collection process can trigger uncomfortable feelings for patients who have experienced trauma.
- Allow patients to make choices about the urine collection process, when possible. For example:
 - Give patients several different options for what time of day the collection will take place.
 - Allow patients to choose which trained staff member will collect the specimen.
- Offer the patient assistance from a peer recovery support specialist throughout the urine collection process.
- Refrain from direct observation of specimen collection. Rather, collection should be

supervised by a staff member. This entails requiring patients to leave their belongings outside the bathroom and to collect their sample without flushing the toilet.

To learn more about trauma-informed urine collection strategies, see Trauma Informed Oregon’s tip sheet, *Trauma Informed Urine Drug Screenings* (<https://traumainformedoregon.org/wp-content/uploads/2019/05/Urine-Drug-Screen-tip-sheet.pdf>).

After the specimen has been collected, laboratory assistants or clinicians collecting urine samples use temperature strips or other methods if specimen tampering is a concern. Urine samples that staff suspect have been tampered with are not sent to the lab for testing. Instead, clinicians or other staff should repeat the urine collection, using the same trauma-informed process.

Encourage participation in mutual-help groups

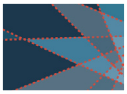
Involvement in mutual-help groups should be encouraged throughout the continuum of care. Patients can be given a schedule of in-person meetings that are easily accessible to them, as well as information about online meetings. Although mutual-help participation has been shown to be associated with positive treatment outcomes (Carroll et al., 2012) and to be helpful for many, it is not a necessary condition for all patients to succeed.

Complete Assessment of Clinical Needs

Assess for co-occurring mental disorders

People with stimulant use disorders, especially people who use MA, may enter treatment exhibiting symptoms of mental disorders. However, not all these patients have a co-occurring mental disorder. Although these symptoms generally subside over several days (for cocaine use) or several weeks (for MA use), some individuals do have a co-occurring disorder.

Psychiatric comorbidity in patients using stimulants is dynamic and should be reassessed throughout the continuum of care. Clinicians need to initiate appropriate treatment, including medication, when patients are experiencing psychiatric symptoms, including psychotic features.



Expressions of suicidal ideation must be taken very seriously. The patient should be monitored for thoughts of self-harm and, when appropriate, provided with immediate intervention to ensure the patient's safety. After the crisis has passed, the clinician and the patient work together to develop a patient-centered safety plan that includes steps the patient can take if suicidal thoughts recur, methods for limiting access to lethal means, coping strategies the patient can use to reduce distress, and contact information for individuals who can help in a crisis (e.g., the patient's clinician, a family member, a close friend, hotlines). (Chapter 6 provides more information on treating co-occurring mental disorders.)

Assess for stimulant-associated compulsive behaviors

Research demonstrates an association between stimulant use disorders and a variety of compulsive sexual behaviors (Berry et al., 2020; Loza et al., 2020). These behaviors may include unprotected anal or vaginal intercourse, transactional sex, compulsive self-stimulation, compulsive seeking and viewing of pornographic material, and more diverse sexual activities and partners than the patient may have engaged in/with previously. Clinicians should screen for the presence of compulsive sexual behaviors in patients with stimulant use disorders.

Patients with stimulant use disorders can have tremendous concerns and anxieties about the compulsive sexual behaviors they engage in while using stimulants. Chemsex is a sexual encounter that is coupled with the use of mind-altering substances during intercourse (Giorgetti et al., 2017). Hypersexuality, sexual assault, and diverse sexual behaviors and partners in the context of stimulant use may result in concerns about sexual identity (Lyons et al., 2010; Ritchwood et al., 2016). When present, these feelings may be barriers to treatment engagement and retention.

Discussions on sexuality with this population must be conducted in a nonjudgmental and caring tone. Clinicians can discuss sexual risk reduction strategies, including initiation of nonoccupational postexposure prophylaxis (nPEP) or pre-exposure prophylaxis (PrEP) for HIV, condom use, serosorting (Centers for Disease Control and Prevention [CDC], 2020a) or seropositioning with partners of an unknown HIV serostatus or serodiscordant partners,

and the need for regular sexually transmitted infection testing of both genital and extragenital (e.g., throat, rectum) sites.

Exhibit 5.1 includes key terms discussed in this chapter.

EXHIBIT 5.1. Key Terms

Serodiscordant: Having a different HIV infection status from that of one's partner.

Seropositioning: The act of choosing a sexual position based on HIV status, such that the partner without HIV is insertive during anal intercourse.

Serosorting: The act of choosing partners with the same HIV status.

Serostatus: An individual's HIV infection status (positive or negative).

Sources: CDC (2020a); Philip et al. (2010).

Studies suggest a link between gambling behaviors and stimulant use, particularly cocaine use, in adults and adolescents (Dufour et al., 2016; Ethier et al., 2020; Geisner et al., 2016). Among a sample of more than 6,000 high school students (Richard et al., 2019), 16.9 percent who reported past-year stimulant use or prescription stimulant misuse were identified as having at-risk/problem gambling. In addition, students who had used any stimulant drug in the past year were 2.7 times as likely to engage in at-risk/problem gambling as those who had not used stimulants. Students with crack cocaine use were 7.2 times as likely, and students with MA use were 8.3 times as likely, to engage in at-risk/problem gambling as those who had not used stimulants in the past year.

Some researchers have suggested that overlap exists between neuroanatomic pathways altered with cocaine use and with gambling behaviors, such as pathways linked to motivation, inhibition, reward processing, decision making, craving, and habit formation (Lorenzetti, 2018).

Resolve Immediate Crises

Patients may enter treatment in physical or emotional crisis. During early treatment sessions, clinicians should reassure patients that SUD services can provide or secure immediate attention to critical

medical and mental health issues. Providing patients with lists of community and mutual-help resources is helpful. These materials should include the names, addresses, telephone numbers, websites, and descriptions of mutual-help groups and resources, medical clinics, social service agencies, food assistance programs, trauma-informed services or services for victims of violence or abuse, temporary housing and shelters, women's shelters, and children's resources. A peer recovery support specialist or case manager can help gather such information and work with patients to follow through.

FOCUSING ON TREATMENT RETENTION

Treatment engagement is critical to getting people into SUD care, but treatment **retention** is equally critical. Simply put, people are less likely to die when in treatment than when not in treatment. Clinicians should not turn away individuals—even those considered likely to drop out from treatment—except in very rare cases. Any amount of time people with stimulant use disorders remain in treatment is an opportunity for them to stay alive and improve their health.

The dropout rate of people in treatment for stimulant use disorders is high (Kampman, 2019). For instance, pharmacotherapy studies of people with amphetamine use disorder report a 40- to 50-percent dropout rate (Lee et al., 2018). People with other SUDs, such as OUD, who also misuse stimulants may be at higher risk for treatment dropout than people with SUDs who do not also misuse stimulants (Tsui et al., 2020).

Using CM may retain people in treatment better than using other psychosocial therapies because it offers them an incentive to stay, such as money or vouchers (Ronsley et al., 2020). But many trials of medication and nonmedication treatments have failed to show a difference in treatment retention between the medication or therapy in question and a placebo or other comparator (Ronsley et al., 2020).

Strategies for Treatment Initiation

During the first several weeks of treatment, individuals may stop or at least reduce their use of stimulants. They may also maintain their use at the

same level during this period. However, these first few weeks can be considered successful if patients have engaged in treatment and taken initial steps to reduce stimulant misuse. Achieving abstinence becomes the focus of treatment engagement after the first 1 or 2 weeks. Although no clear delineation exists between those patients **initiating** abstinence and those **maintaining** abstinence, the initiating period begins 2 weeks into treatment and lasts through 6 weeks of treatment, roughly speaking.

During treatment initiation, the goals are to:

- Identify and break the cycle of compulsive, repetitive stimulant use.
- Initiate a period of abstinence from all substance use.
- Encourage the establishment of behaviors that support abstinence and an abstinent social support network.
- Initiate changes in attitude, behavior, and lifestyle that help maintain abstinence.

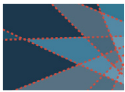
The immediate priorities for facilitating treatment initiation are to:

- Alleviate stimulant withdrawal symptoms.
- Establish structure and support.
- Address secondary substance use.
- Establish contingencies.
- Address compulsive behaviors associated with stimulant use.

Alleviate Stimulant Withdrawal Symptoms

The initial period of stimulant abstinence is characterized by symptoms of depression, concentration difficulties, poor memory, irritability, fatigue, craving for the substance, and paranoia (especially for people with MA use disorder). Among patients who use MA, craving can be present for many weeks or months after achieving abstinence, putting them at high risk for recurrent use in the first few weeks of treatment (Courtney & Ray, 2014).

The severity of these symptoms vary with the severity of use and the route of administration. During the first several weeks of treatment, patients learn that they need proper sleep and nutrition to allow the brain to recover. Giving patients "permission" to



sleep, eat, and gradually begin a program of exercise helps establish behaviors that have long-term utility. Engaging in these behaviors helps patients begin to think more clearly and feel some benefit from their initial efforts in treatment.

Clinicians should continue to encourage abstinence from all illicit psychoactive substances.

ALLEVIATING WITHDRAWAL: CHALLENGING BUT POSSIBLE

Alleviating stimulant withdrawal symptoms is difficult, and withdrawing from stimulants carries a risk of harm to self or others. Fatigue, increased appetite, anxiety, paranoia, and insomnia commonly occur. Medication may provide some symptom relief (particularly for anxiety and sleep disturbance), highlighting the importance of including a psychiatrist or other prescribing professional in the patient's treatment. Rest, relaxation, exercise, and a healthy diet are also "prescribed" to aid in preventing or reducing symptoms.

Other steps clinicians can take to help patients overcome difficulties with withdrawal include (Grigg et al., 2018):

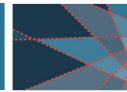
- Alerting patients of symptoms to expect and designing a plan to effectively manage these symptoms.
- Speaking with patients about how to stay motivated throughout the process.
- Monitoring and assessing on an ongoing basis for new or worsening symptoms, including physical symptoms requiring medical attention.
- Treating co-occurring medical and mental health issues as well as polysubstance use; these issues can complicate the withdrawal process.
- Offering supportive care during and after the withdrawal process so that patients receive emotional support and help with maintaining motivation.
- Optimizing sleep hygiene practices.

See the section "Management of Stimulant Withdrawal" in Chapter 3 for additional information.

Establish Structure and Support

Initiating abstinence from stimulant use is not a mental exercise. It requires a specific plan to encourage changes in behavior. The plan provides a basic structure and daily routine to replace the lifestyle dominated by seeking and using drugs and then recuperating from them. Structure, stability, and predictability come from a simple daily plan that patients follow and that is built on the patients' participation in SUD care. This plan includes:

- **Setting short-term goals.** Reasonably achievable, short-term goals are established immediately. One such goal is complete abstinence from all substances for 1 week. To address binge use, a comparable goal is to achieve a period of abstinence approximately twice as long as the usual period between binges. Brief, frequent counseling sessions can reinforce the short-term goal of immediate abstinence and establish a therapeutic alliance between the patient and the clinician. During each session, events of the past 24 hours are reviewed, and the clinician works with the patient to identify goals and provide recommendations for navigating the next 24 hours. Having the patient set up a social support system and undergo urine toxicology screening also contributes to establishing structure, support, and accountability.
- **Maintaining a daily schedule.** Daily scheduling remains an extremely important organizing strategy during treatment initiation. Proactively planning time is a direct counterpoint to the impulsivity people with stimulant use disorder previously experienced. With the clinician, patients review their successes and struggles with the schedule they prepared in the previous session and develop a schedule for the next week. Some patients find this task difficult and resist this "regimentation" of their time. Clinicians may counteract this reticence by creating a strengths-based schedule that celebrates patients' accomplishments for completing daily tasks.



- **Participating in urine testing.** Urine testing is not presented or used as an investigative tool or as a method to test patients' honesty. Rather, it is presented and used as a way to support initiating and maintaining abstinence. SUD treatment providers conduct urine testing for the primary stimulant and for secondary substances during clinic visits. During treatment initiation, urine testing takes place no less than once a week.

Address Secondary Substance Use

People with stimulant use disorders commonly use other substances, such as alcohol or cannabis. They often do not perceive their use of a secondary substance as problematic. Indeed, for many patients, their secondary substance use may not have been associated with adverse consequences or compulsive use. As a result, patients need help connecting any use of other substances to their stimulant use disorder. Patients learn that:

- Using another substance (e.g., alcohol; Staiger et al., 2013) increases the likelihood of recurrent use of the primary substance and treatment nonparticipation (Wang et al., 2017).
- Combining secondary substances of choice, such as opioids or benzodiazepines, with injection drugs (including stimulants) can lead to accidental overdose (Riley et al., 2016).
- Using alcohol with cocaine may increase an individual's perception of euphoria. Some research appears to show that the combination of alcohol and cocaine may be more reinforcing than either substance alone. This combination produces a toxic metabolite—cocaethylene—that can harm the liver and heart (A. W. Jones, 2019; Liu et al., 2018). (For more information about cocaethylene, see Chapter 3.)
- Using low doses and infrequently using secondary substances can have disinhibiting effects, serve as cues for stimulant use, and evoke potent conditioned responses that negatively affect treatment outcomes and retention (Wang et al., 2017).
- Helping patients understand why they use secondary substances can promote behavior change. For example, some patients may use

benzodiazepines, alcohol, or opioids as “landing gear” after a particularly intense stimulant binge. The depressant nature of the secondary substance allows the patient to relax and sleep after several days of prolonged use (Walley, 2013).

Patients are sometimes ready for treatment for their primary substance of choice but are not ready to address their secondary substance use. Thus, secondary substance use is common during treatment initiation. Although clinicians should promote abstinence from all psychoactive drugs, patients who use a secondary substance are not discontinued from treatment solely because of this use. Rather, they receive treatment strategies to decrease the likelihood of using in the future. Patients struggling with more than one SUD need more help, not less.

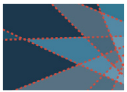
Establish Contingencies

As described in Chapter 4, CM reinforces desired behavior by providing immediate incentives. It can be used to improve treatment outcomes, including abstinence. It sets concrete goals and emphasizes positive behavior changes.

CM targets a specific behavior, such as providing stimulant-free urine samples. The behavior should be easily and objectively measured. Each time patients accomplish this target behavior they receive a specific and desirable contingency or incentive. The link between the target behavior and the incentive is specified. A written contract documents the agreement and the duration, the mechanism for verifying task completion, and any changes over time in contingencies. Controlled research studies show that CM interventions for stimulant use behaviors are effective in helping people who use cocaine achieve and sustain abstinence through the end of treatment at least (De Crescenzo et al., 2018; Ronsley et al., 2020).

Address Compulsive Behaviors Associated With Stimulant Use

As noted above in the section on assessing for stimulant-associated compulsive behaviors, some patients with stimulant use disorders



develop significant compulsive behaviors, such as compulsive sexual behaviors (Berry et al., 2020; Loza et al., 2020) and gambling (Szerman et al., 2020). For these patients, interventions such as cognitive-behavioral therapy (CBT) or mindfulness meditation can be conducted that will decrease the likelihood of both the compulsive behaviors and recurrent stimulant use. Clinicians should provide a safe environment for such patients to talk about these behaviors, either in group sessions or in individual counseling.

Compulsive sexual behavior

Clinicians help patients address compulsive sexual behavior by:

- Helping patients recognize that sexual feelings, thoughts, and fantasies are very high-risk triggers that will be acted upon if they are not talked out. For people who have this problem, even normal, routine sexual thoughts and contacts can quickly become major triggers.
- Discussing safer and unsafe sexual behavior in the context of preventing recurrent behaviors.
- Providing specific and clear recommendations on strategies to identify partners who are low risk for recurrent compulsive behavior (e.g., looking for a partner with no history of substance use, avoiding anonymous sexual encounters).
- Addressing fears (e.g., sex without drugs will be boring or impossible). Many avoidance strategies used with psychoactive substances can be employed for patients in relation to sexual cues as well. For patients engaging in regular or binge patterns of chemsex, the sexual behavior (i.e., seeking a partner, engaging in intercourse, and recuperating) may be as reinforcing as, or more reinforcing than, the stimulant.
- Reminding patients to stay away from people, places, and things related to compulsive sexual behavior. Patients may also need to be reminded to avoid visiting certain neighborhoods where sex workers are located and using the Internet or dating apps to connect with others for sex.

- Providing education about reciprocal behaviors, in which one compulsive behavior is inextricably involved with another, and therefore engaging in the behavior associated with one condition can cause one to act out the behavior associated with the other condition.
- Collaborating with patients to reach the consensus that patients will abstain from sex with other people for 2 to 4 weeks.

Compulsive gambling

Patients with compulsive gambling are likely to respond best to CBT, with some research indicating support for cognitive therapies and MI as well (Potenza et al., 2019). Participating in Gamblers Anonymous provides patients with ongoing support from sponsors and other individuals with similar compulsions.

Harm reduction strategies may be useful for people who are not ready to enter treatment and abstain from gambling. These strategies teach how to engage in gambling with potentially fewer destructive consequences (e.g., limiting time spent in casinos, setting betting limits; Potenza et al., 2019). No FDA-approved medications exist for compulsive gambling.

Strategies for Stabilization

People with stimulant use disorders may be able to discontinue the use of cocaine or MA for periods without treatment. Abstaining from stimulants is the warm-up act; sustaining abstinence is the main event.

Categorizing strategies as being either for achieving abstinence or for maintaining abstinence is somewhat artificial and arbitrary, because many of the same principles apply and many of the same techniques are used over the course of treatment. Several important issues affect stabilization.

After achieving initial cessation of stimulant use, patients need support and strategies to stabilize their lives without the substance. Strategies for this include the following:

- Educate patients about managing subacute and protracted withdrawal symptoms.
- Educate patients about avoidance strategies.

- Provide patient education on factors that contribute to stimulant use.
- Teach basic conditioning.
- Identify cues and triggers.
- Develop action plans for cues and triggers.
- Enlist family participation.
- Help patients establish social support systems.
- Predict scenarios for return to use.
- Establish new activities.
- Respond to early slips.

Educate Patients About Managing Subacute and Protracted Withdrawal Symptoms

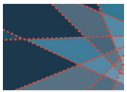
Once a patient discontinues stimulant use and develops healthier sleeping and eating habits, most symptoms collectively described as the “crash” typically lessen. (Chapter 3 provides more information about the crash concept in relation to withdrawal.) But the resolution of crash symptoms does not signal that the brain has returned to normal. Clinical observations show that significant biologic and psychological symptoms continue to hamper functioning 90 to 120 days after discontinuation of stimulant use, a phenomenon sometimes referred to as “the wall.” Symptoms described include mild dysphoria, difficulty concentrating, anhedonia, lack of energy, short-term memory disturbance, and irritability.

The duration of these subacute (between acute and chronic) and protracted (long-lasting) withdrawal symptoms has been a subject of debate. Positron emission tomography scans have provided observable evidence of significant changes in brain functioning, such as decreased glucose metabolism, during protracted abstinence (Parvaz et al., 2011). Although caution about specifying the precise cause or time course of this syndrome is still warranted, neurophysiologic evidence appears to support this phenomenon. Clinicians should educate patients about the subacute and protracted withdrawal symptoms they may experience and when these symptoms may occur. Clinicians can encourage patients to continue using good coping skills to manage these symptoms, including stress management techniques, good sleep hygiene, and healthy eating habits.

Educate Patients About Avoidance Strategies

The process of identifying cues and triggers is dynamic and ongoing and changes over time. For example, as patients learn more about the associations between specific emotional states and stimulant cues, they may become increasingly able to identify, avoid, and defuse potential triggers. Several strategies can be introduced early in the treatment process to help patients avoid certain external or environmental cues that can be potent triggers for stimulant cravings and urges (Kampman, 2019):

- **Discarding drugs, drug paraphernalia, and materials related to substance use.** Patients find and remove all substances (including alcohol) and drug-related paraphernalia. Clinical oversight is imperative to determine the healthiest time to introduce this strategy (i.e., not in the middle of the worst withdrawal symptoms). Patients are encouraged to accomplish this task with the help of a treatment and recovery advocate such as a family member who does not misuse substances, an abstinent friend, a 12-Step sponsor, or a peer recovery support specialist. In addition, they discard materials associated with drug use, such as contact information of people who deal drugs and engage in sex work, pornographic materials, containers used to hold drug supplies, mirrors or special tables used to cut stimulants, spoons, straws or straw-type objects such as pens, razor blades, small or extra-small metal screens, ligatures, syringes not used for medical purposes, and weighing scales. Clinicians should discuss with patients how technology may remind them of past drug use behaviors, and why removing drug-specific content from their computers, mobile devices, and social media can therefore be a good idea. This effort may require an honest discussion with the individual assisting the patient, especially if this individual is not aware of the culture of use the patient was involved in or the patient’s unique patterns and norms (e.g., drug hiding spots, pattern of use at home).



- **Breaking off contact with people who deal and use drugs.** Patients develop plans to stop contact with dealers and other people who use stimulants, including removing contact information and deleting call histories from mobile devices. They also develop plans to assertively encourage family members and close friends who use stimulants to seek help. It may be difficult to break off contact with people dealing and using drugs, because they could be family members or friends. Because of substance use, patients' healthy supports may no longer be in their life and the only supports they have may be people who use and deal drugs.
- **Avoiding high-risk places.** Patients identify places they strongly associate with stimulant use and come up with strategies for avoiding them. Strategies include taking different routes home from work, avoiding certain locations at certain times, and using a buddy system when going to a high-risk area. These high-risk places are sometimes living environments, neighborhoods, or work situations patients cannot avoid.
- **Developing basic refusal skills.** Patients learn to handle encounters with acquaintances and friends who still use stimulants by immediately leaving the situation after an encounter. They also prepare specific drug-refusal statements that they can make during encounters. Patients practice these statements in individual therapy sessions and with fellow group members.

Provide Patient Education on Factors That Contribute to Stimulant Use

Many factors, including cognitive changes, traumatic experiences, and weight gain, may affect patients' memory or perception of their stimulant misuse. Patients may require education to understand the conditioning factors associated with stimulant use. Similarly, they need information about the impact of stimulants and other substances on the brain and behavior, such as cognitive impairment and forgetfulness. Information about stimulant-induced behavior helps explain episodes of mood lability, altered perceptions of reality, protective behaviors, sexual compulsivity, and impulsivity.

Clinicians provide patients, especially those with MA use disorder, with education about acute withdrawal symptoms. Patients should also:

- Learn how other substances they may use have an important role in recurrent stimulant use.
- Receive education about the biopsychosocial processes of SUDs, treatment, and recovery.
- Discuss with their clinicians the stages of treatment and recovery, as well as specific tasks, goals, and pitfalls of each stage.
- Receive education about co-occurring mental disorders and their impact on SUDs, treatment, and recovery.

Teach Basic Conditioning

Although patients with stimulant use disorders may present with poor retention of information and other cognitive deficits early in treatment (Gould, 2010), they should be able to understand basic information about cues and triggers. Patients can be taught that:

- Conditioning factors elicit drug cravings and urges.
- These cravings and urges are a natural part of early recovery and are due to the neurologic changes that occurred from substance misuse.
- Methods are available to deal with these cravings and urges.

Clinicians should provide basic education about this conditioning process and how it applies to stimulant use disorders.

Identify Cues and Triggers

Stimulant (and other substance) use may become strongly associated with certain people, places, objects, activities, behaviors, and feelings (Rawson et al., 2021). Because patients with stimulant use disorders may have engaged in stimulant use hundreds or thousands of times, their daily life contains numerous reminders or cues—any stimuli (e.g., friends who use substances, intimate relationships, locations associated with substance use, drug paraphernalia, seasonal changes, holidays, moods, smells related to the trigger, sex-related websites, stress from increased educational demands) repeatedly paired with substance use

over the course of patients' SUDs. These cues can trigger stimulant cravings and stimulant use. Although patients often have some of the same cues and reminders (e.g., seeing the drug or the dealer), the specific type, strength, and number of cues differ widely from patient to patient. Clinicians should help patients identify and acknowledge the cluster of cues unique to their lives.

The primary tasks are to teach patients how cues are developed, how they trigger drug craving and use, and how cues and triggers can be identified. Cues can be unique to each patient. Patients need to be vigilant about identifying and managing their specific cues.

Develop Action Plans for Cues and Triggers

External and internal cues can be present in every aspect of life for people with stimulant use disorders. To combat these cues, patients can develop action plans with specific behavioral and cognitive steps to prevent cues from becoming triggers. Patients learn to avoid, wherever possible, external cues that are strong reminders of stimulant use and to leave situations that make them think about stimulants or experience cravings. They include these steps in their action plans and call on specific techniques to stop drug thoughts from becoming intense drug cravings.

Strategies that can immediately mitigate stimulant cravings that lead to drug use are vital to sustaining abstinence during stabilization. These strategies include:

- Leaving situations or events that are reminders of stimulant use.
- Using visualization techniques that help “turn off” thoughts about stimulant use.
- Calling a sponsor, recovery ally, or abstinent friend.
- Engaging in activities that promote healthy behaviors (e.g., taking a walk, exercising, using relaxation techniques).
- Using imagery to assist with developing responses to high-risk situations.

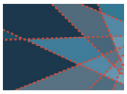
- Recognizing and managing sensory experiences that serve as cues and trigger cravings.
- Maintaining a gratitude list of what has been restored and gained from recovery.

Enlist Family Participation

Clinicians should encourage families and significant others to participate in treatment when appropriate and after receiving patient consent. As part of this participation, families should receive education about SUD care and their possible role in treatment and recovery processes. Family members also need information about the effects of stimulants on the brain and behavior to understand stimulant-induced actions. By receiving a primer on the conditioning aspects of stimulant use disorders, they can come to understand craving as a conditioned response.

Family members may benefit more from clear and simple information than from concepts. The ideal format is a group psychoeducational session consisting of a brief instruction session and a group discussion. This process elicits discussions and examples of family members' experiences. Family participation is an opportunity for staff members to informally review available SUD care in case other family members need additional services or referrals. Family members may benefit from Community Reinforcement and Family Training (CRAFT), which is an approach that teaches family members and concerned significant others strategies for encouraging the family member who is misusing substances to change his or her substance use behaviors through positive reinforcement and enter SUD treatment (SAMHSA, 2020k). For more information about CRAFT, see SAMHSA's TIP 39, *Substance Use Disorder Treatment and Family Therapy* (<https://store.samhsa.gov/product/treatment-improvement-protocol-tip-39-substance-use-disorder-treatment-and-family-therapy/PEP20-02-02-012>).

For patients who are actively working on building their recovery and who have a stable marriage or relationship with someone who is not using stimulants, involving the spouse or partner in family and couples therapy can be valuable.



This strategy can improve communication skills and the relationship. Research shows that marital and relationship counseling has positive effects on treatment outcomes for individuals with alcohol use disorder (O'Farrell & Clements, 2012). However, few studies have focused on stimulant use. Clinicians should screen for intimate partner violence (IPV) before initiating relationship counseling. Behavioral couples therapy is generally appropriate when (SAMHSA, 2020k):

- The partner does not have active problems with substance use (except for nicotine).
- There is no indication of active or acute risk for IPV. The clinician should use clinical judgment and consult state laws on mandatory reporting requirements when evaluating IPV and considering whether to recommend behavioral couples therapy.
- Neither partner has a significant co-occurring mental disorder.
- The partners are married or living together.

(See also the “Family and Couples Therapy” section in Chapter 4.)

Help Patients Establish Social Support Systems

Patients with stimulant use disorders typically have low frustration tolerance and are sometimes restless in the therapeutic process, especially during initiation and stabilization. Nevertheless, these patients should be introduced to a structured and therapeutic group process as soon as possible (generally within a few days). These groups provide a preexisting support network and a forum for openly talking about problems associated with early recovery.

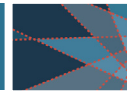
At the same time, participating in mutual-help meetings, such as Cocaine Anonymous, Celebrate Recovery, Crystal Meth Anonymous, Narcotics Anonymous, SMART Recovery, and Wellbriety, should be strongly encouraged. Some patients benefit from short-term goals associated with attending 12-Step meetings, such as participating in 90 meetings in 90 days. Participating in these meetings reinforces the importance of implementing daily structure, immersing in treatment, and creating healthy habits.

Also, patients should be encouraged to reestablish relationships with friends and family who are not using substances and, perhaps, to seek out recovery allies who can be mentors/sponsors. These allies could be 12-Step sponsors whom patients can call during crises to discuss shared experiences in recovery. An abstinent social support network can be a useful tool for patients who need additional support throughout recovery.

Predict Scenarios for Return to Use

Research literature describes several predictors for recurrent stimulant use by patients who are trying to maintain abstinence (Brecht & Herbeck, 2014; Sánchez-Hervás & Llorente del Pozo, 2012):

- **Continued or other drug use leading to recurrent stimulant use and treatment nonparticipation.** Several studies have reported a relationship between alcohol use and recurrent cocaine use, and other studies support this same pattern with alcohol and cannabis for MA treatment nonparticipation (Staiger et al., 2013; Wang et al., 2017).
- **Return to networks of people actively using substances.** The clinical experiences of TIP consensus panel members suggest that returning to networks of people who use substances is a primary reason for an individual's recurrent use.
- **Sexual behavior associated with stimulant use.** Particularly for men, chemsex experiences and sexual behaviors associated with stimulant use (e.g., having sex with sex workers, viewing pornography or sexualized videos of people using substances) are an important contributor to recurrent stimulant use (Berry et al., 2020; Loza et al., 2020).
- **Craving triggered by external and internal stimuli.** People who use stimulants report that conditioned cues have a powerful influence on the production of craving and contribute to a return to stimulant use (Tolliver et al., 2010).
- **Negative affective states.** Emotional states can be important antecedents to recurrent substance use (Kober, 2014). People who use stimulants typically find anger, depression, loneliness, frustration, and boredom difficult to manage. These feelings can initiate a behavioral



sequence that ends in stimulant use. However, celebratory and positive emotions associated with using can also be consequential if they are not identified.

- **Academic demands.** Studies have shown a relationship between prescription stimulant misuse and academic demands among college students (Weyandt et al., 2016), particularly when they have experienced academic impediments or grade strain during the previous academic year (Norman & Ford, 2018). Students who return to school at the beginning of a new academic year and continue to experience academic difficulties may return to misusing prescription stimulants.

Establish New Activities

People with stimulant use disorders typically have spent a considerable amount of time leading up to treatment entry on getting stimulants, using them, and recuperating. During the initial 6 to 12 months of abstinence, patients may not know what to do with the time that they once devoted to substance use. They likely have few social and recreational outlets. Finding and participating in new, positively reinforcing activities and interests are important parts of stabilization and imperative to sustaining recovery. The community reinforcement approach presented in Chapter 4 is an intervention that helps patients reorganize their social lives and engage in new activities.

Respond to Early Slips

Patients may return to stimulant use sporadically throughout stabilization. Patients should be told that substance use could occur during this time, despite their hard efforts to abstain, and that even small treatment accomplishments and successes should be celebrated. Substance use is a part of the disorder and could be a sign that the treatment plan needs to be changed or that the treatment approach is not working and other treatment options should be explored.

During stabilization, substance use is not a sign of poor motivation but instead reflects multiple factors, including cues and triggers and neurochemical imbalance. Slips can be thought

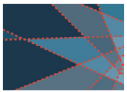
of as a behavioral indicator of conflict and ambivalence about stopping. When explaining this to patients, clinicians need to clearly communicate that they are not giving patients permission to use, but rather, trying to keep patients engaged in treatment by immediately addressing the slip. Continued engagement in treatment throughout stabilization, even if a slip occurs, is the best way for patients to progress and succeed.

Early slips are opportunities for adjusting the treatment plan and trying other strategies. In the process, patients gain an appreciation of the strength of cravings and triggers, learn new methods to manage and reduce them, and examine whether the treatment plan is adequate and appropriate or needs adjusting (e.g., increasing the frequency of contact with their treatment team, attending more mutual-help meetings, spending more time with their sponsor, volunteering).

Early slips should be considered part of the learning process and not be thought of as failures. When slips occur, clinicians make a verbal or behavioral contract with patients regarding short-term achievable goals. These goals include simple tasks such as not using psychoactive substances for the next 24 hours, attending a specific number of clinic sessions over the next couple of days, and bringing a significant other or family member to the next treatment appointment. During this process, patients identify areas to address or improve. This focus on cues and triggers helps determine whether the treatment plan should be adjusted. Reviewing the past day, week, and possibly month of patients' activities, behaviors, and emotions is a good therapeutic tool to identify signs that they were at high risk of substance use.

Strategies for Maintenance

The strategies for maintaining recovery draw primarily from the behavioral and cognitive-behavioral models described in Chapter 4. An overall theme of these models is that people require support even after stabilization to maintain success in treatment.



There are several immediate and long-term priorities for patients who are stable and want to maintain abstinence from stimulants:

- Teach functional analysis of stimulant use.
- Maintain positive reinforcement.
- Teach relapse prevention techniques.
- Provide psychoeducation about preventing a return to use.
- Teach drug refusal skills.

Teach Functional Analysis of Stimulant Use

A functional analysis teaches patients how to understand their stimulant use so that they can engage in solving problems in a way that reduces the probability of future stimulant use. The core components of a functional analysis are:

1. Teaching patients to examine the types of circumstances, situations, thoughts, and feelings that increase the likelihood that they will use stimulants.
2. Counseling patients to examine the positive immediate, but short-term, consequences of their stimulant use.
3. Encouraging patients to review the negative, and often delayed, consequences of their stimulant use.

Maintain Positive Reinforcement

Employing CM agreements can help sustain initial treatment gains. These agreements are detailed in a written behavioral contract and include specific objective criteria such as urinalysis results and attendance at group therapy sessions. Systematic and consistent implementation of agreements is crucial. Reinforcement is delivered promptly when the contract is satisfied and withheld when it is not. Frequent, positive reinforcement of success is critical. Clinicians should always incentivize positive behaviors while trying to avoid punishing negative behaviors because positive reinforcement is a more effective way of shaping behavior than punishment (i.e., punishment can be counterproductive and can lead to avoidance). The goal of positive reinforcement is to encourage patients to continue growing their strengths in recovery rather than to emphasize their struggles.

Teach Relapse Prevention Techniques

Relapse prevention techniques help patients recognize high-risk situations for substance use, implement coping strategies when confronted with high-risk events, and apply strategies to prevent recurring use should an episode of substance use occur (Glasner-Edwards et al., 2017; S. Grant et al., 2017; Marlatt & Gordon, 1985). The techniques involve several cognitive-behavioral interventions that focus on skills training, cognitive reframing, and lifestyle modification.

Relapse prevention techniques fall into several categories:

- Acquiring, through psychoeducation, knowledge about the process of returning to substance use and how to interrupt it
- Identifying high-risk situations and warning signs for a return to use
- Enhancing self-efficacy in dealing with high-risk situations
- Counteracting euphoric recall (i.e., pleasant memories of drug use) and the desire to test control over use
- Developing a balanced lifestyle that includes healthy leisure and recreational activities
- Responding safely to slips to avoid escalation into a full-blown return to use
- Developing coping and stress management skills
- Learning executive function skills
- Learning educational enhancement skills, including time management, study skills, and test-taking strategies

As reviewed in Chapter 4, a substantial body of literature exists on the use of prevention techniques for stimulant use. SAMHSA's Matrix Manual (Center for Substance Abuse Treatment, 2006) has a section on conducting prevention training in a group setting, along with handouts and instructions for their use. The following treatment themes are critical to the relapse prevention-based treatment strategies.

Provide Psychoeducation About Preventing a Return to Use

SUD treatment providers often deliver prevention-related information in psychoeducation groups.

These groups consist of education, peer support, and recovery-oriented therapy. The group leader provides a brief discussion or shows a short video on a topic relevant to the group, then encourages group members to discuss the topic as it relates to them. The group leader also encourages group members to discuss their current problems, challenges, and successes.

Topics typically discussed in a psychoeducation group for patients with stimulant use disorders include:

- Understanding cravings and conditioning.
- Managing protracted withdrawal.
- Understanding stimulants' effects on the brain.
- Identifying and addressing high-risk situations.
- Developing coping and stress-management skills.
- Enhancing self-efficacy in dealing with high-risk situations.
- Counteracting euphoric recall and the desire to test control over use.
- Developing a balanced lifestyle.
- Responding safely to slips to avoid escalation of substance use.
- Establishing behavioral accountability.

Some of these topics are explained below.

Enhancing self-efficacy in dealing with high-risk situations

When patients are establishing abstinence, they work to acquire skills for negotiating high-risk situations for return to use. In particular, patients learn how to identify cues and triggers, develop action plans for cues and triggers, and manage withdrawal symptoms.

Once patients learn to identify, manage, and avoid high-risk situations for return to use, clinicians and patients determine whether patients can confidently use those skills in real-world situations. With clinician guidance, patients evaluate their level of confidence in using avoidance and refusal skills and determine whether they need to work on their skills or develop additional skills to manage specific situations. Self-efficacy should be therapeutically developed from the start of treatment.

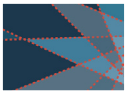
Counteracting euphoric recall and the desire to test control over use

Two important risk factors for return to stimulant use are euphoric recall and the desire to test control over stimulant use. "Euphoric recall" refers to remembering only the pleasures associated with stimulant use and not the adverse consequences. Euphoric recall is a potent risk factor for recurrent substance use because it minimizes patients' perceptions of stimulants' danger, promoting an ambivalence about quitting. "War stories" that include euphoric recall and selective memory act as powerful triggers. Clinicians should strongly discourage patients from retelling them in treatment and recovery groups, unless done in a therapeutic manner directed by the clinician.

After beginning to feel healthier, more in control of their lives, and free of some of their stimulant-related problems, some patients feel ready to try a new approach to stimulant use. For example, some may believe that, if they are careful, they can use stimulants without losing control over their use. Others may think that this is a good time to try using stimulants "one last time" to find out whether they can do it without escalating into compulsive use and loss of control. Even the realization that they do not have money or are in debt may create a desire for "easy money," and patients may think they can sell drugs without using them. Clinicians must explain to patients that urges to test their control over stimulant use are a powerful warning sign for return to use. Patients should reach out to their 12-Step or other mutual-help group sponsor for support if they experience this warning sign.

Developing a balanced lifestyle

Treatment, recovery, and relapse prevention efforts should address biologic, psychological, social, and spiritual areas of life. Patients are taught the value of recreational and leisure activities and how to incorporate them into their recovery. Many recreational activities offer opportunities for patients to learn or practice social skills, such as cooperation, teamwork, healthy competition, and leadership. Patients may be experiencing anhedonia and depressed mood, which could make activities less enjoyable. Clinicians can provide psychoeducation that encourages patients



to take small steps by gently pushing through the anhedonia and depressed mood as long as they are not associated with an untreated or undertreated co-occurring disorder. Clinicians should reinforce that, although it may be difficult to initiate a recreational or healthy leisure activity, patients tend to feel better during and after active participation in the activity.

Vigorous physical exercise helps patients feel good about themselves, decreases anxiety and depression, increases appetite, increases healthy cholesterol, stabilizes blood pressure, increases heart health, and helps patients sleep better. Clinicians inform patients about the value of regular exercise and how to incorporate it into their daily or weekly schedule. Studies on patients receiving MA treatment link structured aerobic exercise and resistance training to better mood outcomes (Morris et al., 2018; Rawson, Chudzynski, Gonzales, et al., 2015) and better overall outcomes (Rawson, Chudzynski, Mooney, et al., 2015).

Patients in treatment for stimulant use disorders may have problems related to nutrition and diet (Wiss, 2019). Stimulants decrease appetite, leading to decreases in the intake of calories and nutrients. Patients with stimulant use disorders may eat impulsively and consume foods with negligible nutritional value. A professional nutritionist can conduct a formal nutritional assessment and provide patients with guidance on eating a healthy and balanced diet, eliminating infrequent and impulsive eating, and planning and preparing nutritious meals. Clinicians should screen patients for eating disorders when clinically necessary, as patients may use stimulants intentionally to facilitate disordered eating behaviors (e.g., suppressing appetite).

Responding safely to slips to avoid escalation of substance use

Slips and episodes of recurrent use are not failures, but they do indicate a need to adjust the treatment plan. After patients experience a slip, clinicians schedule a return-to-use-specific session as soon as possible to reassure patients that they can get back on track. Clinicians and patients review the events leading up to the slip and identify warning signs. Patients consider the events of the previous

weeks, such as changes at work, at school, in social networks, or in family situations. Similarly, they closely examine events and issues that occurred in treatment, such as transitioning to different clinicians, moving from one phase of treatment to another, or learning about or observing events happening to another patient.

Clinicians provide psychoeducation to patients and family members about each stage of change and how their specific characteristics can affect treatment, relapse, and recovery. Clinicians help patients identify specific steps to avoid future substance misuse if a similar set of circumstances recurs. Slips prompt revisions in the treatment plan. Revisions may include increasing attendance at mutual-help meetings, participating in individual counseling for a brief period, recruiting a 12-Step sponsor, developing additional positive coping mechanisms, or participating in more leisure activities. Patients should get recommendations and guidance to handle the negative thoughts and feelings caused by slips.

Teach Drug Refusal Skills

People in recovery from stimulant use may be surrounded by individuals who continue to use substances. The ability to refuse stimulants when offered requires a special type of assertiveness. Drug refusal training reminds patients that anyone offering them stimulants does not have their best interests in mind. Patients learn strategies to discourage others from offering them substances and to refuse offers of stimulants (Meyers et al., 2011). They also learn to reinforce their commitments to abstain from use and to feel good about themselves for not using.

Patients should incorporate the following elements into their encounters with individuals offering them stimulants or inviting them into high-risk situations:

- Say “No” immediately.
- Tell the individual making the offer not to make such offers now or in the future.
- Make eye contact; adopt an expression and tone that indicates the seriousness of the request.
- Change the conversation to a different topic.

- Suggest healthy alternative activities (e.g., go for a bike ride or out for a meal), if the individual is someone the patient wants to be with.
- Set boundaries with friends and family members before meeting with them by establishing that the patient is in recovery and will not use substances.

The clinician conducts role-playing exercises with patients (Meyers et al., 2011) and guides them through scenarios involving specific individuals, specific times of the day, and specific situations. Patients practice behaviors that they can use in real-life situations. Away from the treatment setting, patients should engage in additional role-playing exercises with family members and significant others to become more comfortable with these new behaviors.

Other Strategies Useful in Maintaining Abstinence

Provide Relationship Counseling

The overall goals of relationship counseling (i.e., couples counseling) are for couples to develop effective communication skills to help achieve and maintain abstinence, change their lifestyle, increase enjoyment in their relationship, and learn better ways to solve problems. Information about relationship counseling in the context of SUD treatment can be found in SAMHSA's updated TIP 39, *Substance Use Disorder Treatment and Family Therapy* (<https://store.samhsa.gov/product/treatment-improvement-protocol-tip-39-substance-use-disorder-treatment-and-family-therapy/PEP20-02-02-012>).

Provide Social and Recreational Counseling

This counseling focuses on helping a patient develop new interests and participate in recreational and social activities that do not involve using stimulants or other substances. The clinician and the patient evaluate possible activities based on whether they involve others, how much time and expense they require, whether the patient is likely to enjoy them, and how much physical exertion they require. Potential coparticipants are identified. Next, the steps required to engage in

the activities are identified (e.g., finding out how to join a community basketball league). These steps should be incorporated into the treatment plan.

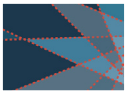
Provide Social Skills Training

Social skills training helps patients learn and practice skills that facilitate choosing nonsubstance alternatives for socializing, engaging in recreation, and coping with stressful interpersonal situations. The goal is to help patients experience more positive reinforcing effects and fewer negative, aversive effects from social interactions. The training is especially helpful for patients who have problems meeting nonsubstance-using peers or interacting with coworkers, or who feel uncomfortable in social settings. Clinicians can use role-playing to help patients learn social skills for use in various scenarios.

Provide Vocational Counseling

Vocational counseling and vocational rehabilitation services focus on helping unemployed patients locate jobs and on improving the employment situations of patients with unsatisfactory jobs or jobs that carry a high risk for recurrent use. Individuals with SUDs may have difficulty finding gainful employment, which can negatively affect treatment-seeking and treatment outcomes (Miguel et al., 2019). In 2017, 31 percent of individuals in the United States admitted to treatment for any SUD were unemployed, compared with 3 percent of the general population (Center for Behavioral Health Statistics and Quality [CBHSQ], 2019). Among individuals who use stimulants, rates of unemployment ranged from 37 to 43.5 percent (CBHSQ, 2019). Research has shown that acquiring employment during SUD treatment is associated with better treatment outcomes throughout the continuum of care (Miguel et al., 2019).

Clinicians should connect patients to vocational rehabilitation services and supports, which can include assistance with job searching, job placement, on-the-job training and supports, costs of living, and other services required for obtaining and maintaining employment (e.g., occupational licenses, tools, equipment; Lusk & Veale, 2018). Ideally, vocational counseling or vocational rehabilitation services should begin as soon as



possible in treatment. However, people in recovery from stimulant use disorders may experience psychotic symptoms and an inability to concentrate that could interfere with initiating vocational services. Vocational services can be initiated after patients' psychotic symptoms have improved and their ability to focus has returned.

For more information about vocational services, see SAMHSA's TIP 38, *Integrating Substance Abuse Treatment and Vocational Services* (<https://store.samhsa.gov/product/TIP-38-Integrating-Substance-Abuse-Treatment-Vocational-Services/SMA12-4216>), and *Integrating Vocational Services Into Substance Use Disorder Treatment Advisory* (<https://store.samhsa.gov/product/integrating-vocational-services-substance-use-disorder-treatment/pep20-02-01-019>).

Provide Treatment and Services To Help Patients Manage Co-Occurring Disorders

Having co-occurring substance use and psychiatric disorders can make achieving and sustaining recovery from stimulant use disorders more difficult. Pharmacologic and psychosocial interventions are available to help patients with common co-occurring psychiatric illness, like depression and anxiety. Clinicians should encourage patients to receive behavioral health services as needed and provide referrals, resources, and support to enhance treatment engagement and retention. Additional treatment considerations for co-occurring disorders are presented in Chapter 6.

Monitor Medications for Treatment of Co-Occurring Alcohol Use or Opioid Use Disorders

When clinically indicated, clinicians use evidence-based medications to treat patients with co-occurring secondary SUDs. Clinicians consult with an experienced SUD treatment provider to determine the best course of pharmacologic treatment for patients based on current use, medical comorbidities, and patient preference.

For patients with co-occurring alcohol use disorder, the FDA-approved pharmacologic therapies

are naltrexone, acamprosate, and disulfiram. For patients with co-occurring OUD, the FDA-approved pharmacologic therapies are methadone, buprenorphine, and naltrexone. For additional treatment considerations specific to OUD, see Chapter 6.

Recommend Mutual-Help Strategies

Mutual-help strategies can be valuable components throughout treatment. These strategies, especially those that focus on substance use, are especially valuable as ancillary activities that support the treatment goals of maintaining abstinence. In general, mutual-help programs assist patients in developing appropriate social skills, creating healthy social networks, establishing healthy intimate relationships, and engaging in substance-free healthy activities. They also provide opportunities for patients to learn socially appropriate mores and norms, improve their ability to receive and give advice, and learn how to mentor others.

The most frequently used and available mutual-help strategy is the 12-Step approach. Most cities have many Alcoholics Anonymous group meetings every day, and most larger cities have numerous Cocaine Anonymous and Narcotics Anonymous meetings. Online meetings are also available. Clinicians or peer recovery support specialists provide patients with information on the 12-Step process, such as meeting format, the spiritual component, the basic content and meaning of the 12 Steps, the role of the 12-Step sponsor, and the role of anonymity.

Although SAMHSA's TIP consensus panel recommends participation in a 12-Step group, clinicians should not require patients' participation. Rather, clinicians encourage 12-Step participation, especially because 12-Step programs describe themselves as voluntary mutual-help programs of recovery. Similarly, patients' family members should be encouraged to participate in mutual-help programs for family members, such as Al-Anon. Scheduling onsite meetings is a good way to encourage participation. Both patients and family members receive lists with the addresses and times of meetings, and programs provide transportation when necessary and possible.

Other mutual-help strategies that do not follow the 12-Step approach are available. These programs include Save Our Selves, SMART Recovery, Wellbriety, and Women for Sobriety. Groups without a substance use focus, such as faith-based groups, cancer survivor groups, and domestic violence survivor groups, can also support patients' progress in treatment.

Next Steps

Treatment maintenance ends only when patients achieve the treatment goals documented in their treatment plans and agree with their clinicians to stop ongoing treatment.

The end of treatment maintenance is a good opportunity for patients to review their treatment experiences. Clinicians engage in activities and exercises that help patients examine their treatment successes, the areas where they experienced problems, and the ways in which they addressed these problems. Similarly, clinicians help patients evaluate the strength of their current recovery process and identify areas where they need strengthening. Through this process, the clinician and the patient develop a continuing care treatment plan that identifies remaining treatment needs and strategies that will be used to meet those needs.

Treatment maintenance ends with a transition to a lower level of care, not a termination. Abrupt termination is avoided. SUD treatment facilities should have strategies that encourage patients to remain connected with care (i.e., using a recovery-oriented system of care), because SUDs are chronic lifelong conditions that can have many pathways to recovery. Furthermore, clinicians should educate patients about the continuity of care available to them and encourage patients to engage with this care when they need it. SUD treatment facilities can help patients remain in contact by offering:

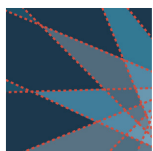
- Continuing care group meetings that patients can attend weekly or more often as needed.
- Individual counseling or psychotherapy that patients can participate in on an as-needed basis.
- Family therapy that is available to patients and their families or to family members.
- Alternative activities that focus on recreation, leisure, education, and social activities (e.g., dances, field trips, barbecues and picnics, holiday events, lectures on topics not necessarily related to treatment or recovery).
- SUD treatment alumni meetings that all graduates can attend.
- SUD treatment alumni clubs that sponsor regional meetings and events (e.g., speakers on motivational and educational issues).
- Peer mentoring programs in which SUD treatment alumni help new patients by sharing experiences, advice, and service expectations.
- Surveys and newsletters that are sent to SUD treatment alumni as a way to collect posttreatment data, encourage participation in alumni activities, and motivate contact with SUD care staff, especially during times of need.

For more information about recovery-oriented systems of care, see SAMHSA's *Recovery-Oriented Systems of Care (ROSC) Resource Guide* (https://www.samhsa.gov/sites/default/files/rosc_resource_guide_book.pdf).

Summary

Clinicians have multiple strategies that they can implement across the continuum of care to maximize patient engagement in treatment for stimulant use disorders. These strategies include discussing treatment expectations, offering multiple treatment options, using a person-centered and respectful approach, conveying empathy and concern, and collaborating with patients to develop a clear, flexible treatment plan and framework. As patients transition to long-term recovery, clinicians can help them maintain treatment gains by teaching functional analysis of stimulant use, reinforcing positive behaviors with incentives (i.e., using CM), offering relapse prevention tools, teaching ways to avoid high-risk situations, providing social skills training, encouraging participation in mutual-help activities, and linking these patients to vocational counseling. Given that patients with SUDs typically have numerous health- and behavioral health-related issues, coordinated care models that include a wide range of multidisciplinary staff can enhance treatment implementation.

This page intentionally left blank.



Chapter 6—Treatment Considerations for Special Populations

KEY MESSAGES

- Populations that experience health disparities related to systems of care and engagement in care may experience higher rates of stimulant use disorder and increased issues with accessing care for stimulant use disorders, and may be more likely to experience secondary negative consequences related to these vulnerabilities (e.g., trauma, communicable diseases).
- Clinicians should strive to understand the needs of special populations, as well as the access-to-care issues and treatment considerations they face. In doing so, clinicians are more likely to provide patient-centered, effective stimulant use disorder care that maximizes rapport and treatment engagement.
- When possible, clinicians should tailor their services to members of special populations to accommodate a given population's particular needs. Examples include having gender-responsive treatment programs for women or programs specifically designed for populations that may experience xenophobia or racism within the healthcare system. Clinicians may need to seek guidance from experts in these special populations when tailoring treatment.

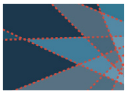
This chapter discusses stimulant use disorder risks and care considerations specific to the following populations:

- Racial/ethnic minorities
- Women (including those who are pregnant)
- Men who have sex with men (MSM)
- Transgender and gender nonbinary (TGNB) community
- Adolescents
- People experiencing homelessness/unstable housing
- Rural populations
- People involved with the criminal justice system
- People taking medication for opioid use disorder (OUD)
- People who inject drugs (PWID)
- People with or at risk for HIV/AIDS
- People with or at risk for hepatitis
- Individuals with co-occurring mental disorders

If a patient with a substance use disorder (SUD) identifies with one or more of these groups, treatment must be informed by a solid understanding of the needs of the group or groups.

Considerations for each special population include:

- Location of treatment centers and community-based organizations.
- Availability of drop-in centers.
- Availability of nonconfrontational programs.
- Treatment approaches that include more time in the engagement phase prior to counseling.
- Treatment that offers individualized approaches, encourages the establishment of safe relationships, allows time for trust to develop, and assesses the level of motivation for change.



- Availability of clinicians trained to help patients identify their own ethnic issues.
- Clinicians matched to patients by cultural understanding (not necessarily racial/ethnic background).

Racial/Ethnic Minority Populations

One of the most important aspects of improving access and developing treatment options for diverse racial/ethnic minority populations is cultural responsiveness in providing care. Cultural responsiveness in the SUD care setting involves clinicians understanding and being responsive to the health beliefs, mores, practices, and values of diverse populations while simultaneously exploring the effects of ethnocentrism and racism on their caring process. For more information on cultural responsiveness, see the Substance Abuse and Mental Health Services Administration's (SAMHSA) Treatment Improvement Protocol (TIP) 59, *Improving Cultural Competence* (<https://store.samhsa.gov/product/TIP-59-Improving-Cultural-Competence/SMA15-4849>). In addition, treatment providers need to understand the culture of their own organization and determine how it may or may not be welcoming to members of other cultures.

Black/African American Populations

This TIP uses the term “Black/African American” to broadly include all people who identify as African American and/or Black in the United States (Center for Behavioral Health Statistics and Quality [CBHSQ], 2020a).

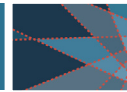
The 2019 National Survey on Drug Use and Health (NSDUH) found that, among Blacks/African Americans age 12 and older, an estimated 1.6 percent (about 521,000) used cocaine and 0.2 percent (about 81,000) used methamphetamine (MA; CBHSQ, 2020a). Compared with people from other racial/ethnic groups, Black/African American populations have had a disproportionately higher risk of cocaine use, cocaine use disorder, frequent

cocaine use, and medical and social problems stemming from cocaine use (Palamar et al., 2015; Zapolski et al., 2016). However, rates of cocaine use among Black/African American adults age 18 and older have been consistently declining in recent years (SAMHSA, 2020b).

MA use has decreased significantly since 2017 among Blacks/African Americans ages 18 to 25, but among those age 26 and older, it leveled off from 2016 to 2018 and then increased by about 24,000 in 2019 (SAMHSA, 2020b). About 2.4 percent of Blacks/African Americans ages 18 through 25 (about 111,000) reported past-year prescription stimulant misuse in 2019, compared with 0.5 percent (about 118,000) of Blacks/African Americans age 26 and older (CBHSQ, 2020a).

The Black/African American community has a history of being arrested, prosecuted, convicted, and imprisoned for offenses involving cocaine (and crack specifically) at higher rates than other racial/ethnic groups and the general population. This is due in part to the 1980s' and 1990s' “war on drugs” approach to prohibiting illicit substances in the United States, which increased the percentage of Blacks/African Americans in state and federal prisons (Dumont et al., 2013).

The strict sentencing laws passed during these decades largely targeted cocaine—and crack cocaine especially. Because crack was more accessible in urban areas than in suburban and rural communities, these stiff sentences resulted in more Blacks/African Americans being incarcerated for cocaine offenses compared with other racial/ethnic groups (Murch, 2015). In fact, crack cocaine carried a federal mandatory minimum sentencing penalty that outweighed powder cocaine—more often used by White Americans—10 to 1 (Murch, 2015). By 2015, the sentencing disparity between crack and powder cocaine was 18 to 1 (Palamar et al., 2015).



STRUCTURAL RACISM AND STIMULANT USE DISORDERS

Beyond developing cultural responsiveness, clinicians also need to be aware of how structural racism, also called systemic racism (that is, racism embedded in social structures and institutions), may be affecting their racial/ethnic minority patients with stimulant use disorders.

Aspects of structural racism and discrimination—like stigma, socioeconomic marginalization, and political bias—have been shown to affect the way healthcare and behavioral health service clinicians diagnose, treat, and interact with people of color (Bailey et al., 2017; Metzl & Roberts, 2014). For instance, the historically disproportionate rates of schizophrenia diagnosed in Black/African American men appear to reflect discriminatory beliefs among clinicians who automatically labeled people with psychosis as aggressive, violent, combative, hostile, and emotionally unstable and who also tended to characterize Black/African American men this way (Metzl & Roberts, 2014). Further, unequal distribution of healthcare resources (e.g., clinics, providers) means people in low-income neighborhoods more often experience a lack of access to high-quality care—or a lack of access to any care—compared with people in higher income areas (Bailey et al., 2017).

One of the most notable historical examples of structural racism affecting people with SUDs can be seen in the response to the crack cocaine epidemic of the 1980s. In the 1980s' "war on drugs," implementation of aggressive policing and harsh sentencing laws for the possession and distribution of crack cocaine differentially affected communities of color and intensified existing social, legal, and healthcare inequalities between Whites and communities of color—notably Black/African American and Hispanic/Latino communities (Rosino & Hughey, 2018). This is in part because crack cocaine possession and distribution were more prevalent in urban neighborhoods—ones less likely to be populated by Whites. Notably, however, lengthier prison sentences are not associated with reduced self-reported drug use, drug overdose deaths, and drug arrests across states (Pew Charitable Trusts, 2018), suggesting that the harsh crack cocaine-related sentencing in the "war on drugs" was not an effective deterrent.

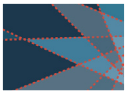
Structural racism persists today within the SUD treatment system (Knight, 2020; Kunins, 2020; Metzl & Roberts, 2014; Rosino & Hughey, 2018). SUD treatment providers and SUD program staff need training not just in cultural responsiveness but in understanding structural racism and unconscious bias so they can better recognize and respond to the barriers facing patients of color (SAMHSA, 2014). Individually, clinicians must be willing to engage in open, nonjudgmental discussions with patients about their racial identities. Such discussions can help clinicians better understand whether and how bias and discrimination are affecting their patients' SUDs and recovery.

Clinicians need to remain present and undistracted during these conversations and be prepared to devote the necessary time and number of sessions to fully exploring issues of racism with their patients. Critical self-analysis is vital to helping clinicians become more aware of their own beliefs and attitudes toward race and the ways they can address structural racism in their own institutions and practices (SAMHSA, 2020i).

On a macro level, clinicians can help transform systemic inequities in the healthcare and behavioral health service systems by (Evans et al., 2020):

- Addressing workforce barriers (e.g., lack of people of color on staff).
- Promoting research, grant-funding, and organizational efforts (e.g., making more of an effort to interview and hire people of color as faculty) for trainees/providers of color.
- Openly recognizing the presence of structural racism and the inequities it has caused and continues to cause.

Behavioral health service clinicians can learn more about structural racism and mental health services by visiting the website of the American Psychiatric Association's (APA) Presidential Task Force to Address Structural Racism Throughout Psychiatry (<https://www.psychiatry.org/psychiatrists/structural-racism-task-force>), which includes continuing medical education programs (for psychiatrists), recommended reading, and video recordings of town halls that address structural racism.



Clinicians working with Black/African American patients should be aware of and sensitive to this difficult history. The “war on drugs” has contributed to the Black/African American experiences of historical trauma, racial bias, and discrimination (Conner, 2020). Black/African American patients may have unresolved grief, deep emotional pain, and strong mistrust related to these experiences, which can create hesitancy to engage with SUD treatment and speak openly about their current or past substance use. Black/African American patients may express hesitancy to initiate treatment for SUDs because of fears about criminal prosecution.

Certain protective factors may help reduce substance use among Blacks/African Americans (Sanders, 2015). Strategies that clinicians can use, as appropriate, to leverage these protective factors include:

- Involving extended family members and nonrelatives with kinship-like ties to the patient in the patient’s recovery when needed and appropriate.
- Incorporating spirituality and spiritual beliefs into treatment, such as using spiritually based coping skills or providing access to SUD treatment in spiritual settings (Jordan et al., 2021).
- Using humor when appropriate.

A sense of belonging to a larger community and a concern for its well-being can also contribute to resilience in Black/African American patients (Sanders, 2015). Clinicians can help build rapport with Black/African American patients and improve their treatment engagement by:

- Acknowledging and empathizing with the historical trauma of racism and discrimination experienced by Black/African American patients (Komaromy et al., 2021; Sanders, 2015).
- Using trauma-informed techniques to manage distress associated with racial trauma that may be perpetuating substance use and impeding recovery, and connecting patients to treatment settings that have a lower risk of retraumatization (Komaromy et al., 2021).

- Being willing to talk about race and racism in sessions (Sanders, 2015).
- Helping patients focus on their strengths and resilience (e.g., talents, support systems, instances from their life where they experienced success) in a system with significant structural racism (Sanders, 2015).
- Giving patients choices and opportunities to make decisions, rather than dictating to them how treatment will go and what will happen (Sanders, 2015).
- Remembering that there are many pathways to recovery, and the one that works best for a particular patient might be different than what works best for other patients (Sanders, 2015).

To learn more about how to work effectively with Black/African American patients who have SUDs (including stimulant use disorders), see SAMHSA’s TIP 59, *Improving Cultural Competence* (<https://store.samhsa.gov/product/TIP-59-Improving-Cultural-Competence/SMA15-4849>), and NAADAC’s free webinar (<https://www.naadac.org/counseling-african-americans-with-substance-use-disorders>) on this topic.

Hispanic/Latino Populations

According to the 2019 NSDUH, 2 percent of Hispanics/Latinos age 12 and older (about 970,000) used cocaine in the past year, and 0.6 percent (about 288,000) used MA (CBHSQ, 2020a). Past-month cocaine use was steady from 2016 to 2019 among Hispanics/Latinos age 26 and older but increased from 1.3 percent in 2018 to 1.6 percent in 2019 among those ages 18 to 25 (SAMHSA, 2020e).

MA use in Hispanics/Latinos ages 18 to 25 declined from 2017 (1.1%) to 2018 (0.7%) and remained relatively unchanged in 2019. However, in Hispanics/Latinos age 26 and older, MA use increased from 2017 (0.6%) to 2018 (0.8%) and then decreased slightly in 2019 (0.7% [SAMHSA, 2020e]).

Prescription stimulant misuse has been steadily decreasing since 2016 (from 5.2% to 3.4% in 2019) among Hispanics/Latinos ages 18 to 25 and has been relatively unchanged (around 0.7%) among those age 26 and older (SAMHSA, 2020e).

The treatment rate for Hispanic/Latino populations in need of SUD care is extremely low, with almost 92 percent of the 3.2 million Hispanic/Latino people age 12 and older with an SUD in 2019 receiving no treatment (CBHSQ, 2020a). There may be several reasons for this gap. Clinicians may not recognize that subgroups of Hispanic/Latino populations—such as Mexicans, Puerto Ricans, Cubans, Central or South Americans, and Spanish individuals—are highly diverse and often differ in their substance use attitudes, behaviors, and ability to access treatment in the traditional medical setting. This heterogeneity is due in part to differences in these subgroups' degree of acculturation, immigration patterns, and geographic location (Chartier et al., 2015; SAMHSA, 2014). These groups may also differ in their race, language, and indigenous ties. All of these subgroup differences might have an effect on treatment engagement, retention, and completion (Chartier et al., 2015).

Language is another barrier for Hispanic/Latino engagement and retention in treatment for SUDs (SAMHSA, 2014). Where possible, SUD care should incorporate multilingual staff and offer culturally appropriate services (SAMHSA, 2014). For example, bicultural care providers have demonstrated improved SUD treatment outcomes for Hispanic/Latino populations (SAMHSA, 2014).

In a small qualitative study of treatment seeking among Hispanic/Latino individuals with SUDs, common reasons people gave for not seeking SUD care were (Pinedo et al., 2018):

- Experiencing cultural barriers, such as feeling as though clinicians did not understand Latino culture or that seeking treatment itself was not acceptable in Latino culture.
- Believing that treatment would not be effective or that clinicians did not have a lived experience with substance use problems and thus could not effectively help the patient.
- Not wanting to pursue abstinence, but rather, harm reduction (e.g., limiting intake).
- Feeling as though treatment was unnecessary because functioning did not seem impaired (e.g., no substance-related work absences, no significant family problems related to substance use).

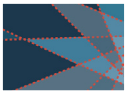
- Fearing stigma (e.g., being seen as “weak” by others for seeking treatment).
- Lacking family support for treatment.
- Experiencing logistical difficulties (e.g., no health insurance; long waits to be seen by a clinician).

Clinicians can overcome some of these barriers and help improve treatment outcomes for Hispanic/Latino patients by (Pinedo et al., 2018; SAMHSA, 2014):

- Learning about Hispanic/Latino culture and subcultures and understanding how substance use and accessing treatment are viewed within each.
- Incorporating Hispanic/Latino cultural values and concepts into sessions, such as *familialismo* (valuing the family and its needs over that of any one individual) and *respeto* (showing respect to a person based on their age and gender).
- Emphasizing the scope (and also limitations) of confidentiality. This might be especially important for a patient who is undocumented and who may worry that being open and honest about substance use could lead to deportation.
- Being creative in service delivery to help the patient avoid stigma and to protect the patient's privacy and anonymity. For instance, clinicians might want to offer web-based treatment when possible and appropriate, or consider integrating services within a primary care setting.
- Including the patient's family in sessions—with patient permission—when needed and appropriate.
- Offering harm reduction and recovery-oriented services beyond those focused only on abstinence.

Asian and Native Hawaiian and Other Pacific Islander Populations

In 2019, an estimated 1.1 percent (about 174,000) of U.S. Asians and 2.8 percent (about 31,000) of Native Hawaiians and Other Pacific Islanders (NHOPI) age 12 and older engaged in past-year cocaine use; far fewer—0.1 percent of Asians (about 19,000) and 1.5 percent of NHOPI (about



16,000)—reported past-year MA use (CBHSQ, 2020a). An estimated 1.0 percent (about 159,000) of Asians and 0.8 percent (about 9,000) of NHOPI age 12 and older engaged in past-year prescription stimulant misuse (CBHSQ, 2020a).

Past-month use of cocaine in Asians and NHOPI ages 18 to 25 fell markedly from 2016 (about 33,000) to 2017 (about 1,000) and then rebounded in 2018 and 2019 (to about 25,000 and 21,000, respectively). In Asians and NHOPI age 26 and older, past-month cocaine use decreased between 2017 and 2019, down to about 52,000 in 2019 (SAMHSA, 2020d).

Regarding past-year MA use, a significant drop occurred from 2016 to 2017 (about 9,000 to less than 500) in the 18-to-25 age group, with rates stabilizing in 2018 and 2019 to around 9,000 and 8,000, respectively (SAMHSA, 2020d). Asians and NHOPI age 26 and older reported less past-year MA use in 2019 (about 26,000) than in 2018 (about 35,000 [SAMHSA, 2020d]).

Past-year prescription stimulant misuse by Asians and NHOPI ages 18 to 25 increased from about 81,000 in 2017 to 137,000 in 2018 and then dropped back down to 87,000 in 2019 (SAMHSA, 2020d). For individuals age 26 and older, rates have been fairly consistent, staying somewhere between 60,000 and 101,000 from 2016 to 2019 (SAMHSA, 2020d).

Although the prevalence of substance use in general is low among Asians and NHOPI collectively, the annual SUD treatment admission rate of this group grew more than those of non-Asian and non-NHOPI populations from 2000 to 2012 (Sahker et al., 2017). But for MA use specifically, treatment admissions in this population increased by only 12 percent during this time, and rates for cocaine use treatment actually decreased by almost 51 percent (Sahker et al., 2017). Additionally, in 2019, only 7 percent of Asians/NHOPI age 12 and older with any past-year SUD received treatment (CBHSQ, 2020a). Notably, a study found that Asians and NHOPI who use MA were less likely to complete treatment compared with Whites who use MA (Godinet et al., 2020). Collectively, these data suggest that greater efforts

are needed to address SUD treatment access, engagement, retention, and completion in Asian and NHOPI populations—especially among those with MA or cocaine use disorders.

ASIAN AND NHOPI POPULATIONS AND STIMULANT USE DISORDER STATISTICS

It is important to recognize the diversity of Asian and NHOPI populations when considering the prevalence of stimulant use disorders. This is in part because the percentage of people in the United States who identify as Asian American (5.7%) is much larger than the percentage who identify as NHOPI (0.2%; U.S. Census Bureau, n.d.). Grouping Asian and NHOPI populations together can lead to interpretations of data that obscure the needs of NHOPI and underrepresent the impact of stimulant use and prescription stimulant misuse on NHOPI individuals.

Asians are sometimes considered “model minorities,” referring to the false belief that a minority group largely possesses only positive qualities. This stereotype contributes to a misperception that Asians do not engage in substance use (Kim, 2021; Sahker et al., 2017). Consequently, individuals who are aware of this misperception—and feel pressure not to defy it—may hesitate to seek SUD treatment when needed. Also, clinicians may be less likely to look for substance problems in this population (Sahker et al., 2017).

Other possible treatment barriers include (Masson et al., 2013):

- Worry that SUD care will not be culturally tailored or linguistically appropriate.
- Fear of stigma and losing face (in Asian and NHOPI cultures, one’s social standing, reputation, dignity, and honor) if people—especially family members—find out help was sought from “outside” rather than from within the family.

- A lack of support (emotional, financial, or tangible) from family members who may not believe that treatment is necessary and may even be using substances themselves.

Additionally, Asians and NHOPI comprise numerous subgroups (e.g., Chinese, Japanese, Indian, Vietnamese, Hmong, Samoan) that have different attitudes toward and beliefs about substance use and treatment seeking (SAMHSA, 2014). Further, across these subgroups, individuals differ on level of acculturation and immigration status—two factors that have been linked to the presence of SUDs and their type. For example, higher degrees of acculturation have been linked to a greater risk of drug use disorders than have lower degrees of acculturation (Salas-Wright et al., 2015). Understanding these differences between and within subgroups can help clinicians better understand individual patients' feelings and beliefs about substance use and SUD treatment. For more information, see SAMHSA's TIP 59 (<https://store.samhsa.gov/product/TIP-59-Improving-Cultural-Competence/SMA15-4849>).

The following strategies may further help Asian and NHOPI patients with stimulant use disorders initiate, participate in, and complete treatment (SAMHSA, 2014):

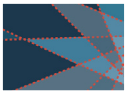
- Culturally adapted SUD care (e.g., clinicians discuss presenting issues using patients' culturally based explanations of them, rather than imposing views that could negatively affect patients' attitudes toward treatment) and, where available, services in patients' preferred language might help patients feel more understood by the clinician.
- Shame can be a treatment barrier for Asian and NHOPI populations, so establishing warm and supportive clinician–patient relationships can help reduce feelings of embarrassment and encourage acceptance of treatment.
- During the initial session, clinicians can help build patient confidence in their expertise by using their title, displaying diplomas and training certificates, and discussing their experience working with other patients with stimulant use disorders.

Clinicians working with Asian and NHOPI women with MA use should be especially mindful of screening for and addressing co-occurring disorders (CODs) as well as providing services or referrals to help with relationship issues and vocational challenges. This suggestion is based on a comparison of Asian/Pacific Islander men and women in treatment for SUDs (Han et al., 2016) in which MA was the primary drug for more than half of the women in the study. Women in the study were more likely than male participants to report significant family/social relationship problems, employment difficulties, and mental health issues.

American Indian and Alaska Native Populations

An estimated 6.9 million people identify as American Indian or Alaska Native (AI/AN), and 1.6 million AI/ANs are younger than age 18 (U.S. Government Accountability Office, n.d.). AI/ANs have the highest rates of SUDs of any U.S. racial/ethnic minority population, with 10.2 percent of AI/ANs age 18 and older meeting criteria for an SUD (CBHSQ, 2020a).

Recent NSDUH data show a decline in cocaine and MA use among AI/AN adults and a slight increase in prescription stimulant misuse among AI/AN adolescents and young adults (CBHSQ, 2020a). The rate of past-year MA and cocaine use in people age 12 and older (1.9% and 1.4%, respectively) remains high compared with other racial and ethnic groups (Baldwin et al., 2020; CBHSQ, 2020a; SAMHSA, 2018a). MA is the most prevalent drug seized from AI/AN communities, primarily owing to easy access and low prices associated with abundant distribution from large, well-organized drug trafficking organizations located in nearby border towns (*To Protect and Serve*, 2019). In a study examining prescription stimulant misuse in adolescent American Indians, nearly 7 percent of the sample had been prescribed stimulants and nearly 6 percent of the sample reported misusing stimulants to get high (Spillane et al., 2017).



Awareness of the following considerations can assist clinicians in providing culturally responsive care for AI/ANs with stimulant use disorders:

- Most AI/ANs believe that historical trauma, including the loss of culture, lies at the heart of SUDs within their communities (SAMHSA, 2018a).
- Because of the diversity among AI/AN cultures, clinicians with AI/AN patients should consult with professionals who are experienced in working with members of the specific tribes to which patients belong (SAMHSA, 2014).
- Use of substances often begins at a younger age than it does in other major racial/ethnic groups (R. A. Brown et al., 2016; SAMHSA, 2018a).
- Two-spirit individuals reported higher rates of illicit drug use, alcohol use, and mental health service use than their cisgender counterparts (“cisgender” refers to people who identify with the gender that matches their birth sex) in a small study conducted among urban AI/ANs (Balsam et al., 2004). “Two-spirit” is a pan-Indian term referring to AI/AN people combining activities of both men and women with traits unique to their status as two-spirit people, and who, in most tribes, were traditionally regarded as an alternative gender (Indian Health Service, n.d.). Among AI/AN people, the term can also be used to describe sexual orientation.
- Increased rates of suicidal ideation and suicide attempts have also been reported in a study evaluating the impact of boarding school attendance on mental health issues and substance use among urban two-spirit individuals (Evans-Campbell et al., 2012).
- There are multiple barriers to accessing SUD care in the AI/AN community, some of which include physical distance from service providers, concerns about maintaining anonymity, shame and prejudice, lack of childcare and transportation, a limited number of culturally competent AI/AN providers, and mistrust of government-funded social services (SAMHSA, 2018a). A full list is available in SAMHSA’s TIP 61, *Behavioral Health Services for American Indians and Alaska Natives* (<https://store.samhsa.gov/product/TIP-61-Behavioral-Health-Services-For-American-Indians-and-Alaska-Natives/SMA18-5070>).
- AI/AN communities experience higher rates of trauma compared with other racial groups, especially among AI/AN women. Trauma exposure (including violent crime, intimate partner violence, child abuse, violence against two-spirit individuals, and injuries) increases the risk for substance use (Baldwin et al., 2020; Ehlers et al., 2013; SAMHSA, 2018a).
- Resiliency factors in AI/AN communities are rooted in cultural traditions, family support, and cultural pride (LaFromboise et al., 2006).
- Practice-based approaches (knowing what works through experience, clinical judgment, cultural knowledge, and patient feedback) are much better accepted in AI/AN communities than evidence-based practices are (SAMHSA, 2018a).

Clinicians should also be mindful of patterns of urbanization among some AI/AN populations—especially patterns of forced migration into urban areas due to factors like land dispossession and natural disasters—and how this relocation might affect their patients. Some AI/AN populations living in urban areas—especially youth—may experience a weaker cultural identity, less cultural involvement, and more acculturative stress than AI/AN populations living on reservations or in rural AI/AN communities. These experiences could negatively affect their mental health and substance use behaviors (R. A. Brown et al., 2016). Some AI/AN patients living in urban areas face unique challenges related to SUD care, such as limited access to Indian Health Service care and culturally appropriate SUD treatments (Tonigan et al., 2020; Whitesell et al., 2012).

A national survey of urban and rural SUD treatment programs that provide services to AI/AN populations (Rieckmann et al., 2016) found that rural programs had a higher mean number of years of staff experience, were more likely to offer open mutual-help recovery groups (e.g., Alcoholics Anonymous), and were less likely to have traditional healers and ceremonial providers among their staff, but were more likely to have elders working in their program.

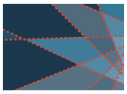
Although clinicians should strive for cultural understanding, nontribal clinicians should not practice traditional healing when treating AI/AN patients of a given tribe. Rather, clinicians “should rely on the community and native tribal council (governance) to guide the selection of traditional practitioners and the integration of traditional healing practices across the continuum of care” (SAMHSA, 2018a, p. 8). Clinicians should first ask AI/AN patients about their desire to incorporate cultural beliefs and practices into their treatment, as some may not have an interest in doing this (SAMHSA, 2014, 2018a).

Examples of cultural responsiveness in practice include:

- Addressing barriers to SUD care. Clinicians conduct needs assessments to identify and tailor services based on community strengths and resources, provide one-stop services, offer “warm-handoffs” to bridge referral gaps, develop outreach and community events that incorporate education and promote engagement, utilize telehealth services, and form partnerships between states and tribes (Baldwin et al., 2020; SAMHSA, 2018a).
- Recognizing AI/AN communication styles, such as the use of (1) nonverbal messages to convey respect or displeasure, (2) humor to ease psychological pain or discomfort with difficult topics, (3) indirect communication to avoid criticism of others and the appearance of being disloyal or disrespectful, and (4) stories to deliver personal messages (SAMHSA, 2009). Clinicians can enhance communication by listening and respecting silence, adjusting eye contact, asking questions about nonverbal cues, anticipating laughter, determining and valuing linguistic preferences and abilities, and using hopeful language and avoiding labeling (SAMHSA, 2018a).
- Addressing harmful narratives that result from historical trauma by offering AI/ANs the chance to explore the role of culture, history (including historical trauma), acculturation, discrimination, and bias in their stimulant use (SAMHSA, 2018a).
- Integrating holistic approaches that focus on mind, body, spirit, and context, particularly during the transition from adolescence to adulthood (Friesen et al., 2015).
- Including AI/AN communities in research and program design, development, implementation, and dissemination to ensure that AI/AN-specific issues are adequately represented in culturally sensitive interventions and prevention programs (Baldwin et al., 2009).

Clinicians may find using a traditional, Western approach to SUD treatment is too individualistic and lacks a focus on concepts like belongingness and a sense of community identity, which tend to be highly valued in AI/AN populations (Walsh-Buhi, 2017). Western treatment approaches may also fail to contextualize SUDs in this population in terms of their culture’s unique history, the presence of historical trauma, ongoing poverty and its effects, and the collective trauma experienced by this population as a whole (Walsh-Buhi, 2017). Neglecting these important contextual factors may make SUD treatment less effective for certain AI/AN patients (Walsh-Buhi, 2017).

For more information on culturally responsive SUD care for AI/AN patients and a list of culturally adapted SUD treatment approaches, see TIP 61, *Behavioral Health Services for American Indians and Alaska Natives* (<https://store.samhsa.gov/product/TIP-61-Behavioral-Health-Services-For-American-Indians-and-Alaska-Natives/SMA18-5070>). See also the resources available through the SAMHSA-funded National American Indian & Alaska Native Addiction Technology Transfer Center (<https://attcnetwork.org/centers/national-american-indian-and-alaska-native-attc/home>).



THE IMPORTANCE OF THINKING ABOUT SOCIAL DETERMINANTS OF HEALTH

Health is much more than just one's physical condition. To truly understand why a patient is struggling with a physical or behavioral health problem, such as a stimulant use disorder, a clinician needs to consider the full picture of social and environmental factors that contribute to the formation and persistence of health issues.

Social determinants of health (SDoH) have been defined as “the conditions in the environments where people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks” (Healthy People 2030, n.d.), including risk for substance misuse and related health consequences (Office of the Surgeon General, 2016).

Common examples of SDoH include (Andermann, 2016; Healthy People 2030, n.d.):

- Poverty or income insecurity.
- Homelessness or housing instability.
- Food insecurity.
- Racism and discrimination.
- A history of childhood physical, sexual, or emotional abuse.
- Joblessness.
- The air and water quality in one's living environment.
- The safety and stability of one's neighborhood.
- Access to healthcare and behavioral health services.
- Access to education.
- Access to nutritious food.
- Access to transportation.

SDoH have been implicated in SUD formation and treatment access and completion (Sanner & Greene, 2020). For instance, an analysis of data from the 2012 NSDUH found the presence of several SDoH significantly increased an adult's odds of having lifetime MA use, including (King et al., 2019):

- Having a family income of less than \$20,000/year.
- Not having had a job in the previous 12 months.
- Having participated in a government assistance program in the previous 12 months.
- Having a high school education or less.

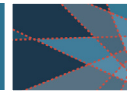
Clinicians need to ask patients about—and identify—possible SDoH that could be playing a role in their substance use. Not doing so could make it difficult—or even impossible—to get some patients to enter and remain in recovery. And patients' answers can reveal the need for “social prescribing” (Andermann, 2016)—that is, linking the patient to social services or referrals for any SDoH in the patient's life that are amenable to change (e.g., referring the patient to vocational rehabilitation, coordinating care with a social worker who can help enroll the patient in federal food or housing assistance programs).

Some SDoH—like poor air and water quality, racism and discrimination, and neighborhood crime—are not easily modifiable by a clinician or any patient affected by them. But simply understanding that such factors are present in a patient's life can help a clinician adopt a more empathic and nonjudgmental approach to SUD care.

Other strategies for clinicians include (Andermann, 2016):

- Developing cultural responsiveness as a critical pathway to learning how to identify and talk with patients about SDoH, particularly factors like racism, stigma, discrimination, immigration and acculturation, and inequities.
- Taking a person-centered, trauma-informed approach to SUD care. This includes not just learning how to ask patients about sensitive topics like abuse, violence, and other trauma but also about deeply personal topics like job or housing loss, immigration concerns, or literacy difficulties.
- Considering how to make treatment more accessible for all patients (e.g., offering evening hours, providing bus vouchers for patients relying on public transportation).
- Becoming advocates at the community, state, or national level to help enact social change, promote healthier communities, and support health equity.

For more information about SDoH and screening tools that can be used for assessment of SDoH, see the Rural Health Information Hub's Social Determinants of Health in Rural Communities Toolkit (<https://www.ruralhealthinfo.org/toolkits/sdoh>).



Women (Including Those Who Are Pregnant)

Treating stimulant use disorders in women can be significantly more complicated than treating stimulant use disorders in men because of the complex social structures and biases that women experience in their daily lives. Roles associated with motherhood, such as childcare, pregnancy, breastfeeding, and care of elder family members, may increase the familial responsibilities of women with SUDs. Power structures that are patriarchal in nature may complicate a woman's road to recovery through intimate partner violence, assault, and socioeconomic disenfranchisement. Additionally, data suggest that sexual minority women experience increased rates of stimulant use compared with their heteronormative counterparts (Philbin et al., 2020).

In a study examining co-occurring SUDs and posttraumatic stress disorder (PTSD), women who used cocaine only or in combination with cannabis had increased rates of repeated traumatic exposures, including arrests, incarceration, and adult sexual assault compared with women who used cannabis only (Ruglass et al., 2017). Additionally, cocaine use among women is related to increased stress associated with family obligations for which they do not receive additional help (Preston et al., 2018). The risk for suicide among women veterans with cocaine use disorder is significantly higher than for men veterans, indicating the presence of CODs and further complicating treatment considerations (Bohnert et al., 2017).

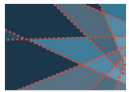
Although men and women use MA at similar rates, women often begin using MA at an earlier age and develop dependence more quickly than men (E. E. Hartwell et al., 2016). Additionally, women are more likely to obtain MA from a significant other and to use MA to assist with weight loss and enhanced energy (E. E. Hartwell et al., 2016). Women with MA use disorder have more psychiatric comorbidities (e.g., depression and anxiety), but tend to have longer treatment retention and better treatment outcomes (E. E. Hartwell et al., 2016).

There are several indirect entry points into the SUD treatment system for women, including:

- Pediatricians (mothers may take children to the doctor even when they do not go themselves).
- Child protective services.
- OB/GYN providers.
- Social service agencies.
- Primary care providers.
- Criminal justice agencies.

Barriers to effective evidence-based treatment are multifactorial for women. Access to care is a major barrier, particularly for women in rural settings. Among parenting women with SUD, women in rural settings had 90-percent lower odds of receiving treatment compared with urban women (Ali et al., 2020). Another study that considered women experiencing homelessness who were seeking services for their SUD found that a significant portion were highly motivated for treatment, but physical and transportation barriers remained an issue in accessing care (Upshur et al., 2018). Additionally, these women identified feeling depressed as the primary barrier to seeking services. Given that women in treatment for stimulant use disorders have a higher risk for PTSD (Saunders et al., 2015), it is important to consider the role this comorbidity may play in decreasing engagement in care for women. Women who had been arrested in the last year were 3 times as likely to receive treatment for their SUD as were women who had not (Martin et al., 2020).

Another barrier to effective care for women with a stimulant use disorder is the effect of self-stigma and previous traumatic medical experiences related to their SUD. Particularly among pregnant or parenting women, self-stigma related to their ability to parent or care for their children may cause them to avoid treatment situations that worsen feelings of shame or guilt (Cockroft et al., 2019; Frazer et al., 2019). SUD care should focus on engaging women and creating a safe and strengths-based treatment program to avoid further stigmatization of a vulnerable population.



The five core components of gender-responsive care are:

1. Addressing women's unique experiences.
2. Using a trauma-informed approach.
3. Using relational approaches.
4. Addressing women's needs in a comprehensive manner.
5. Providing a healing environment.

Treatment for women should use a holistic, gender-responsive approach. Topics could include:

- Relationships with family (after addressing social functioning, issues of homelessness/unstable housing, social isolation).
- Treatment needs of children.
- Intimate partner violence.
- Parenting.
- Life skills.
- Education and vocational training.
- Economic self-sufficiency.
- Reproductive health issues.
- Education about long-term effects of using stimulants.
- Mental health.
- Self-esteem.
- Independent living skills.
- Nutrition.
- Transportation.
- Ethnic and cultural issues.
- Day care and group counseling for children.

Transactional/survival sex (sex offered in exchange for tangible goods or services, like money, drugs, food, or shelter) is not a phenomenon exclusive to women who use stimulants; it is a concept that providers need to understand and discuss with their patients. More than 40 percent of women with a cocaine use disorder who were in outpatient SUD treatment have engaged in transactional sex; more than 10 percent continue engaging in these behaviors even in the setting of abstinence from cocaine (Rash et al., 2016).

Clinicians should address the specific needs of women who engage in—or who have previously engaged in—transactional/survival sex using

a trauma-informed approach to develop care plans. For women who continue to engage in transactional sex work, developing safety plans, avoiding cues and triggers related to substance use, and promoting health and reproductive autonomy may increase engagement and improve outcomes (Ditmore, 2013).

Pregnant Women and Their Children

National estimates of stimulant use among women of reproductive age show high rates of prescription stimulant misuse (617,000), followed by cocaine (540,000) and MA (317,000; CBHSQ, 2020a). The rate of stimulant use in the general population continues to rise and is mirrored in the rate of use among pregnant women (Smid et al., 2019).

The prevalence of cocaine use during pregnancy has been difficult to quantify but is estimated at 1.1 percent at any point in pregnancy (Bhuvaneswar et al., 2008; Forray & Foster, 2015), with up to 750,000 exposed pregnancies and births each year (Cain et al., 2013). Results from the 2019 NSDUH showed that 0.2 percent of pregnant women reported past-month cocaine use (CBHSQ, 2020a). Cocaine use is a major cause of antepartum hospitalizations related to substance use among pregnant women (Smid et al., 2019).

Data on the prevalence of MA use in pregnancy also are limited, although national estimates range from 0.7 to 5.2 percent (Forray & Foster, 2015), and rates continue to rise, primarily in rural areas of the South, Midwest, and West. In a national sample of hospital deliveries occurring between 2004 and 2015, approximately 82,000 deliveries were affected by maternal amphetamine use, reaching a peak of 2.4 per 1,000 amphetamine-related hospital deliveries between 2014 and 2015 (Admon et al., 2019). Stimulant use during pregnancy is underreported and selective screening based on race or socioeconomic status may miss patients and children that could benefit from more tailored interventions (Martin et al., 2020; Smid et al., 2019). The prevalence of prescription stimulant misuse during pregnancy is not fully known. In 2019, NSDUH data showed that between 1 and 5.2 percent of reproductive-age women reported misuse of prescription stimulants (1.4% of women

ages 12 to 17, 5.2% of women ages 18 to 25, and 1 percent of women age 26 and older; CBHSQ, 2020a).

Effects on Pregnant Women

Stimulant use during pregnancy is associated with numerous harmful physical and psychological outcomes. Cocaine is toxic to multiple organ systems and can cause high blood pressure, heart attack, kidney failure, rupture of the liver, reduced blood flow to the heart and brain, strokes, seizures, and death (National Institute on Drug Abuse [NIDA], 2016b; Smid et al., 2019). As a result, cocaine toxicity can mimic preeclampsia (Cain et al., 2013). Cocaine use during pregnancy has a well-documented association with placental abruption (premature detachment of the placenta from the uterus) and preterm birth (Elkafrawi et al., 2020). Further, cocaine interacts with hormonal changes (e.g., increased progesterone) during pregnancy, which can worsen cardiovascular toxicity (Smid et al., 2019). Infection transmission is another risk of prenatal cocaine use, as women can transmit HIV, hepatitis, and syphilis to their fetuses. Women who misuse prescription stimulants during pregnancy can experience similar detrimental health effects, including high blood pressure, placental abruption, premature delivery, and postpartum hemorrhage (Worley, 2014).

MA has similar physiologic effects on pregnant women and is strongly associated with poor oral health and increased risk for infectious diseases, such as hepatitis and HIV (Smid et al., 2019). Studies have shown increased risk for miscarriage, stillbirth, placental abruption, and uterine rupture due to MA use. Stimulant use during pregnancy also has psychological consequences. A longitudinal study examining physical and psychological outcomes of prenatal cocaine use found poorer perceptions of mental health, higher rates of PTSD, and higher rates of other substance use among pregnant women with cocaine use compared with pregnant women without such use (Minnes et al., 2012). The study also demonstrated that prenatal cocaine use strongly predicts perceived psychological distress up to 10 years postpartum (Minnes et al., 2012). Similarly, pregnant women who misuse prescription drugs including stimulants have an increased risk

for psychosocial consequences, including poor judgment, impaired decision making, violence victimization, inadequate housing, involvement with the legal system, poor engagement in prenatal care, and co-occurring mental disorders (Worley, 2014).

Perinatal, Neonatal, and Developmental Effects

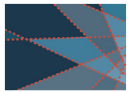
Cocaine can cross the blood–brain barrier and the placenta. Prenatal cocaine use increases the risk for (Dos Santos et al., 2018; Gouin et al., 2011; Smid et al., 2019):

- Placental abruption.
- Premature delivery.
- Low birth weight.
- Small-for-gestational-age infants.
- Earlier gestational age at delivery.
- Fetal growth restriction.

Although studies documenting long-term outcomes of fetal cocaine exposure are limited, there is evidence showing effects on children that include problems with behavior (e.g., difficulties with self-regulation), growth, inhibitory control, attention, and information processing (NIDA, 2016b; Smid et al., 2019). Cocaine can be passed to an infant through breastmilk; thus, breastfeeding is another source of exposure.

MA use during pregnancy also has detrimental effects on fetuses, such as earlier gestational age at delivery, lower birth weight, and smaller head circumference (Smid et al., 2019). After birth, infants who were exposed to MA in utero can experience withdrawal symptoms, such as jitteriness, drowsiness, and respiratory distress (Smid et al., 2019). Neurotoxicity is much higher with prenatal MA use than prenatal cocaine use (Dinger et al., 2017), leading to a range of long-term neurodevelopmental problems in childhood. Prenatal exposure to MA is associated with (Dinger et al., 2017; Smid et al., 2019):

- Aggression.
- Anxiety.
- Depression.
- Poorer motor performance.



- Lower IQ scores.
- Increased likelihood of cognitive problems affecting academic achievement.
- More problems with peers.

Less is known about misuse of prescription stimulants among pregnant women. However, studies of pregnant women taking prescription stimulant medications for attention deficit hyperactivity disorder (ADHD) have shown small increased risks for preeclampsia, premature delivery, and placental abruption (Smid et al., 2019).

Pregnant women should be screened for substance use, including stimulant use. Screening approaches can include brief self-report tools, brief intervention and referral to treatment screening methods, and urinalysis, following consent and appropriate counseling (American College of Obstetricians and Gynecologists [ACOG] Committee on Health Care for Underserved Women, 2011). Clinicians should be aware that many pregnant women are reluctant to admit or disclose stimulant use out of fear of losing custody of their children (A. O'Connor et al., 2021), highlighting the need for showing empathy and building rapport. Additionally, clinicians should expect to encounter women with diagnosed ADHD that may or may not be treated and women with undiagnosed ADHD (Marraccini et al., 2017).

Pregnant women who use stimulants require comprehensive prenatal care that is gender responsive and tailored to their needs (Chin & Bartholomew, 2020). This care should include nutritional assessment, testing for sexually transmitted infections and HIV, and access to social support services (ACOG, 2011). Given that stimulant use during pregnancy can impair fetal growth and increase the risk for pregnancy loss, pregnant women who use stimulants should have frequent ultrasounds and monitoring of fetal health throughout pregnancy, as clinically indicated (ACOG, 2011). Clinicians should ensure that these patients have established care with an OB/GYN and are connected to the appropriate ancillary services.

Patients taking prescription stimulants for ADHD should discuss with their healthcare providers the risks and benefits of using these medications while pregnant. Continued use of prescription stimulants

may be warranted in patients with severe ADHD symptoms that interfere with daily functioning (Marraccini et al., 2017). However, patients with milder forms of ADHD that do not significantly affect daily functioning may wish to discontinue their prescription stimulants while pregnant and engage in psychosocial treatments, such as cognitive-behavioral therapy (CBT).

ACOG (2011) recommends that pregnant women who are unable to stop using MA or other stimulants seek SUD care. Given the importance of SUD treatment in the context of pregnancy, pregnant women should voluntarily seek care at a residential treatment center whenever possible. If residential treatment is not possible, outpatient therapy sessions should be frequent for at least 90 days after treatment initiation. Treatment interventions should include:

- Patient and family education about the dangers of stimulant use to both mother and fetus.
- Motivational interviewing to assess readiness for change.
- Contingency management (CM) with tangible incentives to encourage treatment initiation and retention and reduced stimulant use.
- CBT, used in the Matrix model and trauma-focused therapy.
- Mutual-help support.
- Drug testing to monitor drug use and treatment progress.

Stressors and psychological distress during the postpartum period may increase the risk for relapse, necessitating close follow-up and support after delivery (ACOG, 2011; Smid et al., 2019).

Clinicians should also help connect pregnant women with stimulant use disorders to peer recovery support specialists, where available. Peer recovery support specialists are individuals with a lived experience of SUD recovery who are specially trained, supervised, and often certified to provide nonprofessional, nonclinical supportive services for other people with SUDs. The lived experience aspect is a critical piece of what helps make peer recovery support specialists effective in their work, as this experience conveys to patients a deep sense of understanding and empathy. Use of peer recovery support specialists has been linked to

many positive outcomes in SUD recovery, including increased abstinence, reduced substance use, better SUD treatment adherence and completion, and improved engagement in long-term recovery support, like mutual-help services and continuing care participation (Fallin-Bennett et al., 2020).

Little research to date has focused on the use of peer services for pregnant women in recovery from SUDs. However, existing evidence suggests peer recovery support specialists likely can offer pregnant women with SUDs a sense of trust, support, understanding, and connectedness (Fallin-Bennett et al., 2020; Paterno et al., 2018) that might help them later access and stay in recovery.

For additional information on substance use issues in women's health and pregnancy, see these SAMHSA publications: TIP 51, *Substance Abuse Treatment: Addressing the Specific Needs of Women* (<https://store.samhsa.gov/product/TIP-51-Substance-Abuse-Treatment-Addressing-the-Specific-Needs-of-Women/SMA15-4426>); *Guidance Document for Supporting Women in Co-ed Settings* (<https://www.samhsa.gov/resource/ebp/guidance-document-supporting-women-co-ed-settings>); *Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants* (<https://store.samhsa.gov/product/Clinical-Guidance-for-Treating-Pregnant-and-Parenting-Women-With-Opioid-Use-Disorder-and-Their-Infants/SMA18-5054>); and *Preventing the Use of Marijuana: Focus on Women and Pregnancy* (<https://www.samhsa.gov/resource/ebp/preventing-use-marijuana-focus-women-pregnancy>).

Men Who Have Sex With Men

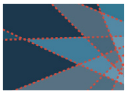
Nationally representative data on MSM and their substance use patterns are not currently available. But based on individual studies, MSM may have a high rate of stimulant use. For instance, among MSM ages 16 to 20 surveyed from 2009 to 2013, 6.2 percent reported lifetime use of cocaine and 3.3 percent reported recent cocaine use, whereas 1.1 percent reported lifetime MA use and 0.7 reported recent MA use (Newcomb et al., 2014). Other researchers have estimated higher rates, particularly for MA use, which has ranged from about 21 to 27 percent in other studies of MSM (Anderson-Carpenter et al., 2019). Among a sample of 286 MSM who use MA, 31 percent

reported a co-occurring cocaine use disorder (Fletcher et al., 2018). Using NSDUH data, a 2021 study evaluating prescription drug misuse by sexual identity found that men who identified as gay or bisexual had higher rates of past-year prescription stimulant misuse (5.1% and 6.4%, respectively) compared with men who identified as heterosexual (2.3%; M. Diaz et al., 2021).

MSM with HIV may be especially at risk for stimulant use. In a study of 766 MSM with HIV, more than one-third (35%) reported having used cocaine, crack, crystal MA, amphetamine, and/or ecstasy in the previous 3 months, and of these, 40 percent reported using injection drugs (Teran et al., 2020).

MSM may be at an increased risk for intimate partner violence, self-stigma/internalized homophobia, and trauma—all of which may be associated with negative health consequences, like depression, and could increase their likelihood of using substances (Batchelder et al., 2017; Duncan et al., 2018; Lopez-Patton et al., 2016; Moody et al., 2018). Some MSM—such as those experiencing homelessness or unstable housing—may engage in transactional sex, which has been linked to an increased risk of substance use and HIV infection and transmission (especially with casual as opposed to regular partners [Bauermeister et al., 2017]). In a study of MSM with and without HIV, among those who reported transactional sex, 60 percent reported using MA and 13 percent cocaine (Javanbakht et al., 2019).

MSM are at an increased risk of HIV acquisition compared with the general population. In 2019, MSM made up 69 percent of new cases of HIV diagnosed in the United States (Department of Health and Human Services, 2021). Among the population of MSM, two factors affecting the risk of acquiring HIV are race and age. For example, from 2015 to 2019, MSM ages 25 to 34 accounted for the largest number of HIV diagnoses attributed to male-to-male sexual contact (Centers for Disease Control and Prevention [CDC], 2021a). In 2019, the percentage of HIV infections caused by male-to-male sexual contact was somewhat higher in Black/African American (82%) and Hispanic/Latino (87%) males compared to White males (73%; CDC, 2021a). Research has found that MSM who use stimulants are more likely to engage in



condomless sex or to engage in other behavior—like forceful penetration that can lead to condom breakage—that increases the risk of transmission or infection with HIV (Vu et al., 2015; Yu et al., 2015).

Sexual risk-taking often occurs under the influence of substances. Sexual risk-taking within the context of substance use is hypothesized to occur because of the disinhibitory effects of the drug, learned patterns (especially between stimulant use and certain high-risk sexual practices), low self-esteem, altered perception of risk, lack of assertiveness to negotiate safer practices, and perceived powerlessness (Bourne & Weatherburn, 2017; Ritchwood et al., 2015; Semple et al., 2011; Thompson & Auslander, 2011). Substance use can reinforce risky sexual behavior through enhancement of sexual pleasure (Bourne & Weatherburn, 2017; Ritchwood et al., 2015). Young MSM report misusing prescription stimulants to increase sexual desire (Kecojevic et al., 2015).

A wide range of factors, including sexual activities with an increased risk of HIV acquisition, likely contribute to the increased odds of HIV infection related to substance use among MSM (Edelman et al., 2016; Schneider et al., 2013). Other possible contributors to increased risks of HIV infection, especially among younger MSM, include (CDC, 2014):

- Misinformation about HIV prevention strategies and difficulty in accessing highly effective forms of prevention and treatment, particularly among racially and ethnically diverse MSM (Mayer et al., 2020; Ojikutu et al., 2018).
- Lack of widespread, effective education about HIV prevention and treatments among MSM.
- Missed opportunities for HIV testing to increase patients' knowledge of their HIV serostatus and help them appropriately access and engage in care.
- Lack of awareness among some MSM with HIV about their positive HIV status and about safe sexual practices to limit the spread of infection.
- Feelings of rejection and loneliness among some MSM who may experience marginalization, bullying, harassment, and estrangement from family or friends, sexual victimization, or the intersectionality of homophobia and racism (CDC, 2014).

There currently are no clear data on rates of SUD treatment seeking among MSM in the United States. An Internet survey conducted in 2008 found that only 3 percent of MSM surveyed had accessed drug or alcohol treatment in the past 60 days (Hirshfield et al., 2015). A 2017 literature review that analyzed findings from the United States, the United Kingdom, and Australia suggests that SUD treatment rates among MSM are likely much lower than they are among men who identify as heterosexual and do not engage in sex with other men (Bourne & Weatherburn, 2017).

One treatment study looking at stimulant use in MSM is Project IMPACT, an HIV risk reduction and behavioral activation counseling intervention for MSM without HIV who are currently using stimulants (Mimiaga et al., 2018). Study researchers hope to determine whether 10 weekly sessions of education for HIV risk reduction, CBT for substance use reduction, and behavioral activation to improve mood, reduce substance use, and enhance motivation to engage in HIV risk reduction behavior will result in fewer instances of condomless anal sex without the protection of preexposure prophylaxis (PrEP), relative to a control group. Findings from the study have not yet been published.

In the absence of data, it is difficult to know for certain the barriers that prevent more MSM who need SUD treatment from seeking it, and thus how clinicians and treatment facilities can help overcome these barriers. A lack of specialty SUD care for MSM may be a major deterrent, as clinicians not trained in working with this population may not understand the unique challenges facing some MSM and the sociocultural issues that may contribute to substance use among them (Bourne & Weatherburn, 2017).

SUD treatment clinics may find success in reaching, engaging, and retaining MSM patients by adapting strategies recommended for healthcare service delivery programs that address the specific needs of MSM. These strategies include offering (United Nations Population Fund [UNFPA], 2015):

- Flexible clinical hours and services (e.g., emergency medication pickups, walk-in services).

- Services that address specific adversities facing MSM (e.g., sexual assault, intimate partner violence, physical assault, abandonment).
- Referral to community-based and social services.
- Welcoming, nonhostile tone toward MSM and their needs (staff training is key).

The term “men who have sex with men” is an all-encompassing term to identify specific behaviors rather than label someone’s sexual orientation. Recently, with changes in stigma toward the lesbian, gay, bisexual, transgender, queer, and intersex+ community, many patients feel comfortable sharing their gender identity and sexual orientation with clinicians or the outside world. Still, stigma persists, and fears of marginalization and homophobia—particularly in the healthcare setting—contribute to whether patients wish to disclose or self-identify their sexual orientation. Patients may choose to keep this information confidential or request that the information not be shared in the medical record, as they fear what could happen if they were ever “found out.” This may be an indicator of a larger need to address self-stigma or previous trauma with the medical system.

Clinicians should understand that MSM may self-identify in different ways, and that this is a diverse population. Some MSM may consider themselves gay, and others may identify as heterosexual or bisexual (UNFPA, 2015). Yet other MSM may not be comfortable self-identifying in any particular way.

Stigma and fear of physical or emotional harm may keep some MSM from feeling comfortable discussing themselves and any struggles they may have encountered, which can be a challenge to getting them to enter SUD treatment (UNFPA, 2015). When clinicians can help MSM feel comfortable sharing information about their self-identity and sexual behaviors, it may have positive effects in terms of reducing their risk of HIV. Among MSM, disclosure of same-sex practices to healthcare providers has been associated with an increased likelihood of undergoing HIV testing (Qiao et al., 2018). Healthcare settings in which MSM are more likely to disclose include ones in which physicians are perceived to be younger in age and nonhostile toward the gay community

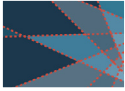
(Qiao et al., 2018). Specific barriers to disclosure include:

- Healthcare providers’ failure to ask patients directly about their sexual practices.
- Patients’ fear of their confidentiality being violated.
- Patients’ fear of stigma.

Internalized homophobia and self-stigma can perpetuate ongoing substance use. Patients who have always associated same-sex contact with shame and guilt may use substances to pacify those feelings so that they can engage in the activity. Strategies to help patients through self-acceptance, and remittance of internalized homophobia, particularly for those who are not “out,” may be an important aspect of helping patients achieve recovery and minimize drug-related problems (Moody et al., 2018).

PWID make up only a small portion of positive cases of HIV in the United States. In 2018, of the more than 37,000 people newly diagnosed with HIV in the United States, about 10 percent were PWID (CDC, 2021b). However, injection drug use is still concerning because it can increase risk of HIV transmission or can be associated with sexual behaviors that could make HIV transmission more likely. For instance, a study of MSM with HIV who use MA showed that negative attitudes about condoms and higher levels of MA use are associated with higher levels of unprotected anal sex (Nakamura et al., 2011). Conducting risk assessment, including analyzing patients’ use to see how sex fits into their use patterns, is critical for clinicians and outreach workers to do.

Clinicians should ask patients about their sexual activity and whether they are taking antiretroviral medication as PrEP. Research suggests that gay and bisexual men who indicate a willingness to adopt PrEP for HIV prevention may also be willing to engage in more risky sexual behavior, like decreasing or stopping condom use during anal sex (Brooks et al., 2012). However, among MSM specifically, the relationship between PrEP use and increased risky sexual activity is not clear and requires further study (Freeborn & Portillo, 2018). This underscores the importance of talking openly with patients about their use of PrEP



and subsequent sexual behaviors and ensuring that they understand that having risky sex while adopting PrEP could negate the HIV-prevention benefits of PrEP by exposing them to other

sexually transmitted infections. Patients should be both counseled on this risk and offered additional HIV risk reduction and prevention strategies (e.g., behavioral counseling, access to condoms).

CHEMSEX AND STIMULANT USE DISORDERS

Chemsex, also known as sexualized drug use, is a sexual encounter that is coupled with the use of mind-altering substances before or during intercourse to facilitate, enhance, prolong, and sustain the sexual experience (Giorgetti et al., 2017; S. Maxwell et al., 2019). In addition, using substances to reduce cognitive inhibition during sexual encounters can increase perceptions of confidence and emotional connection (S. Maxwell et al., 2019). Despite these expected benefits, some research has shown that this disinhibition can increase risk-taking behavior and negatively affect psychosocial functioning, especially when multiple substances are used (Closson et al., 2018; S. Maxwell et al., 2019).

Historically, cannabis, ecstasy, amphetamine, and cocaine were the substances most commonly used in chemsex; however, γ -hydroxybutyric acid (GHB) and congeners, mephedrone, MA, erectile dysfunction agents, alkyl nitrites, and ketamine have become increasingly used in sexual encounters (Giorgetti et al., 2017; S. Maxwell et al., 2019). Using substances during sexual encounters can occur in a variety of settings (e.g., saunas, sex-on-premises venues, private homes). Phone applications and online platforms have made it easier for individuals to locate and connect with others who engage in chemsex.

Among U.S.-based studies that have focused on chemsex and stimulant use, the prevalence of MA use ranged from 9 to 22 percent (S. Maxwell et al., 2019). International and U.S.-based studies have shown cocaine to be the least frequently used chemsex drug, with prevalence estimates ranging from 2 to 33 percent (S. Maxwell et al., 2019). Studies with large samples of MSM found that between 1 and 9 percent reported injection drug use, with MA being the most commonly injected substance (S. Maxwell et al., 2019).

Chemsex is well described among MSM (S. Maxwell et al., 2019). Research remains limited, and prevalence rates vary greatly by geographical location and culture (S. Maxwell et al., 2019). MSM who engage in chemsex are most likely to be White, identify as gay, and be between the ages of 32 and 42 (S. Maxwell et al., 2019).

The use of chemsex drugs during sex has been shown to increase engagement in high-risk sexual behaviors (e.g., condomless anal intercourse) in MSM, which, in turn, increases the risk of acquiring sexually transmitted infections and HIV (S. Maxwell et al., 2019). Studies examining the use of nPEP (nonoccupational postexposure prophylaxis) and PrEP among MSM who participate in chemsex remain extremely limited.

Clinicians who work with individuals using stimulants can assess for chemsex-related behaviors by asking the following screening questions:

- Have you ever thought about using substances when having sex?
- When was the last time you had sex while using substances?
- Have you ever felt guilty about what you have done under the influence when having sex?

Transgender and Gender Nonbinary Community

In the United States, approximately 0.3 percent of adults identify as transgender (Stroumsa, 2014). In a study of adults age 18 and older who self-identified themselves as within the gender spectrum or gender variant, 45.2 percent identified as neither male nor female, and 5.5 percent identified as both male and female (Kuper et al., 2012). Further, 72.3 percent of participants identified with more than one current gender identity (e.g., male, female, genderqueer, transgender, transsexual, crossdresser, two-spirit, bigender, intergender), with a reported average of 2.5 gender identities (Kuper et al., 2012).

Exhibit 6.1 includes key terms discussed in this chapter.

EXHIBIT 6.1. Key Terms

Cisgender: A term that refers to individuals who do not identify as transgender. These individuals' gender identities, expressions, and roles align with the sex assigned to them at birth and the culturally established categories of gender.

Transfeminine: Individuals who were assigned male at birth but identify with the feminine side of the gender spectrum or as nonbinary.

Transgender: An umbrella term for individuals whose gender identities, expressions, and roles occur on a continuum, often differ from the sex assigned to them at birth, and cut across culturally established categories of gender. Understanding of the transgender community continues to evolve. Therefore, some patients and health professionals may define “transgender” slightly differently.

Transmasculine: Individuals who were assigned female at birth, but who identify with the masculine side of the gender spectrum or as nonbinary.

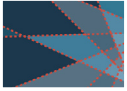
Sources: American Psychological Association (2015); Center for Substance Abuse Treatment (2012); Coleman et al. (2012); Human Rights Campaign (n.d.); Mayo Clinic (2017a); Scheim et al. (2017).

Most substance use research with the TGNB population has focused on alcohol use. Significantly fewer studies have assessed the prevalence of illicit drug use. Results from these studies show cocaine and amphetamine use is somewhat more common among transgender people than cisgender people, with past-year cocaine use among transgender people an estimated 6.8 percent higher and past-year amphetamine use an estimated 1.3 percent higher (Scheim et al., 2017). A study of SUD treatment programs in San Francisco, CA, demonstrates that transgender identity predicts MA and injection drug use in women (Flentje et al., 2014).

Benotsch and colleagues (2013) found that among transgender individuals who misused prescription drugs, 13.5 percent misused prescription stimulants. Prescription drug misuse has been shown to be more common among binary transgender men, nonbinary individuals assigned female at birth, and nonbinary individuals assigned male at birth compared with binary transgender women (Kidd et al., 2021).

Stimulant use patterns differ between transgender and cisgender populations. Past-year cocaine use is higher among transmasculine individuals, and past-year amphetamine use is higher among transfeminine individuals compared with use among cisgender men and women (Scheim et al., 2017).

Substance use, particularly injection drug use, among the TGNB population increases the risk for transmission of blood-borne diseases such as HIV and hepatitis. A large multinational study of HIV infection rates among transgender women in the United States, Europe, Latin America, and the Asia-Pacific region showed the odds of being infected with HIV are 49 times higher among transgender women compared with all adults of reproductive age, regardless of race, culture, or socioeconomic status (Baral et al., 2013). The high rate of HIV infection among transgender women is concerning, given the barriers that TGNB individuals face in accessing care.



Transgender individuals with any lifetime treatment for substance use tend to be older and transfeminine, access gender-affirming health care, and have lower income levels (despite higher education levels). Seeking treatment for recent substance use is associated with a history of mental illness-related risk factors (e.g., being a victim of intimate partner violence and experiencing PTSD and depression) and with engagement in mental health services (Keuroghlian et al., 2015). Additionally, treatment for recent substance use is associated with participating in sex work, having unstable housing, and experiencing discrimination related to public accommodations (Keuroghlian et al., 2015).

Several factors contribute to the development of SUDs and use of treatment services among TGNB people. People who identify as transgender have a higher risk for verbal, physical, and sexual victimization and frequently encounter interpersonal and structural discrimination (Keuroghlian et al., 2015). A national survey of transgender individuals found that 28 percent of individuals delayed medical care because of discrimination and barriers such as (J. M. Grant et al., 2011):

- Refusal of care (19%).
- Harassment in medical settings (28%).
- Violence in medical settings, including physical assault in a doctor's office (2%).
- A lack of provider knowledge about trans-affirmative care (50%).

Transgender individuals report using substances to cope with stigma and mistreatment (J. M. Grant et al., 2011), ultimately increasing the odds of alcohol, cannabis, or cocaine use by 3 to 4 times and, among transgender women, any drug use by 8 times (Nuttbrock et al., 2014). Co-occurring mental disorders (e.g., depression, PTSD) also can increase the risk for substance use and facilitate the underlying relationship between gender-related violence and substance use (Nuttbrock et al., 2014; Rowe et al., 2015).

Data from several studies from the 2000s suggest that approximately 50 percent of transgender individuals with SUDs do not seek treatment because of concerns about stigma (Matsuzaka, 2018). When

seeking inpatient SUD care, TGNB people encounter structural barriers, such as gender-segregated treatment facilities, institutional bias, and stigmatizing attitudes among providers (Matsuzaka, 2018).

Research on interventions for reducing problematic substance use in the transgender community remains scarce and has largely consisted of feasibility and acceptability studies conducted in the context of risky sexual behavior and HIV transmission (Glynn & van den Berg, 2017). But increased understanding of TGNB issues affecting general healthcare delivery has contributed to the American Psychological Association's formulation of TGNB-specific recommendations for mental health service and SUD care delivery.

In 2015, the American Psychological Association recognized ongoing advancements in TGNB-informed research and published practice guidelines to assist clinicians with providing culturally responsive, developmentally appropriate trans-affirmative care. When working with the TGNB population, clinicians should have foundational knowledge and awareness of the spectrum of gender diversity, cultural backgrounds, and life experiences (e.g., stigma, discrimination, violence victimization) of TGNB people to provide individualized, TGNB-specific health care (American Psychological Association, 2015). Clinicians should help TGNB patients by (American Psychological Association, 2015):

- Providing a safe environment to explore gender identity and expression, while recognizing their own attitudes and beliefs (e.g., asking for preferred pronouns, displaying TGNB-affirmative resources, adapting paperwork that includes demographic information).
- Learning about TGNB-specific topics that affect care.
- Acknowledging the existence of institutional barriers that can delay treatment engagement.
- Remaining nonjudgmental.
- Modeling acceptance.

Learn more about clinical considerations when treating TGNB patients with SUDs in SAMHSA's *A Provider's Introduction to Substance Abuse Treatment for Lesbian, Gay, Bisexual, and*

Transgender Individuals (<https://store.samhsa.gov/product/Providers-Introduction-Substance-Abuse-Treatment-Lesbian-Gay-Bisexual-Transgender/SMA12-4104>).

Adolescents

Substance use among adolescents is of critical concern because of its associations with their physical and social development. Hormonal surges during puberty, especially in testosterone, support risk-taking behaviors, which can be negative (e.g., underestimating the danger of drinking and driving) or positive (e.g., trying out for a sports team or a role in a play). Adolescent years are also a time of expansive cognitive development (e.g., emergence of abstract reasoning, robust memory) and increased focus and specialization (Silvers et al., 2019). In essence, the adolescent brain is laying down a network of cognitive pathways that will shape and guide future brain development and, thus, adult thinking and behavior.

Adolescence is a time of social maturation as well. Cultural expectations are that young adults emerge from adolescence with enhanced autonomy—ready to separate from their families, further their education or find employment, and begin to establish an independent existence. One aspect of this increased focus on the self can be, paradoxically, increased susceptibility to peer influences, for good and ill.

Because the brain is undergoing intense and rapid change during adolescence, it is particularly vulnerable to the effects of substance use. Substance use during adolescence is associated with abnormal brain development, including poor cognitive performance (Otten et al., 2019). Cocaine and MA use and amphetamine misuse during adolescence have been shown to rewire still-developing parts of the brain and alter the functioning of more mature parts (Salmanzadeh et al., 2020).

Many substance misuse prevention and treatment efforts are directed at teenagers because intervention during adolescence can help prevent SUDs in later life. One of the strongest associations with substance use before age 15 is the development of SUDs in later adolescence and adulthood (Otten et al., 2019). Early substance use

is also strongly associated with depression, suicidal ideation, and suicide attempts among adolescents (Marschall-Lévesque et al., 2017).

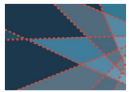
Despite the negative effects that adolescent substance use has on physical and mental health, most problems with substance use resolve without any treatment as people enter adulthood (Cousijn et al., 2018). When considering the vulnerability of adolescents to substance use, it is helpful to remember that they also show remarkable resilience. The same plasticity that makes their developing brains particularly susceptible to the ill effects of substance use also seems to equip adolescents to learn and adapt.

According to nationally representative data (CBHSQ, 2020a; University of Michigan, 2020):

- More than one in three students (34.7%) in 8th, 10th, or 12th grade have used an illicit drug, including cannabis. That figure climbs to almost one in two (46.6%) if surveying only 12th graders.
- Regarding cocaine use, 2.6 percent of 8th, 10th, and 12th graders surveyed had ever used cocaine (including crack cocaine); 1.4 percent had used cocaine in the previous year.
- Among people ages 12 to 17, an estimated 75,000 engaged in lifetime MA use.
- Among people ages 12 to 17, about 430,000 engaged in past-year prescription stimulant misuse.

Adolescent usage rates for cocaine, amphetamines, and MA have been dropping for two decades. In 1999, nearly 1 in 10 high school seniors had tried cocaine (9.8%), 1 in 6 had used amphetamines (16.3%), and 1 in 12 had used MA (8.2%; Johnston et al., 2020).

Despite declining use, stimulants warrant attention for at least two reasons. First, adolescents tend toward polysubstance use, estimated at 12 to 34 percent among this group depending on age and setting (Kecojevic et al., 2017). Per NSDUH 2019 data, people age 12 and older with past-year MA use are 4 times as likely to use cannabis, 2 times as likely to drink heavily, 9 times as likely to misuse prescription opioids, and 17 times as likely to use cocaine as those with no past-year MA use (CBHSQ, 2020a). Second, they tend to



use substances that are convenient to obtain; thus, rates of stimulant use are likely to be higher in areas with ample availability. Nationwide, when 12th graders were asked about availability of various stimulants, more than a quarter (28.4%) said it was fairly or very easy to obtain cocaine; availability of powder and crack cocaine was roughly equal (18.3% and 16.5%, respectively; University of Michigan, 2020).

Few adolescents who need treatment for stimulant use disorder receive it. According to 2019 NSDUH data, only 0.5 percent of adolescents receive treatment for any SUD (CBHSQ, 2020a). By some estimates, SUD treatment reaches less than 6 percent of the adolescents who need it (Silvers et al., 2019).

The advantages of identifying substance use problems in adolescents and intervening successfully are significant. Most people who develop an SUD will do so in adolescence or young adulthood (Saitz et al., 2021). Identifying adolescents who are using substances can help prevent those individuals from developing SUDs later in life. Drug and alcohol use are the primary preventable risks that contribute to some of the leading causes of death for adolescents—namely, accidents, homicide, and suicide.

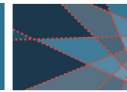
The American Academy of Pediatrics' clinical report, Substance Use Screening, Brief Intervention, and Referral to Treatment (<https://pediatrics.aappublications.org/content/138/1/e20161211>) provides information about substance use screening and treatment for adolescents.

Adolescents may be inclined to use prescription stimulants in a nonprescribed way or use another person's prescription to try to improve cognitive and academic performance (Benson et al., 2015; Weyandt et al., 2016). Stressors including college entrance exams, school assignments, and familial pressure may make misusing prescription stimulants appealing. All adolescents should be screened for stimulant use disorder regardless of academic performance or other perceived achievements. Notably, there is no evidence that taking stimulants prescribed by a medical provider for the treatment of ADHD in adolescence leads to the development of SUDs in adulthood (Quinn et al., 2017; Wilens et al., 2011).

Risk-taking behaviors are not limited to substance use in adolescence. Increased sexual risk-taking behaviors can occur in adolescence more generally, especially when adolescents demonstrate high levels of sensation seeking and impulsive decision making (Charnigo et al., 2013). Clinicians caring for adolescent patients with stimulant use disorder should conduct a careful sexual health history to identify potential needs, including screening for sexually transmitted infections, PrEP/nPEP (nonoccupational postexposure prophylaxis) referral, or additional education about safe sex practices.

Evidence-based SUD treatment seems to be less effective for adolescents than for adults. This may be partly because many evidence-based treatment approaches are developed for and tested primarily on adult populations. A review of 29 studies of interventions to prevent adolescent substance use found that interventions that were successful in reducing or preventing illicit substance use were narrowly targeted (e.g., addressing only Asian American girls, eighth-grade girls in foster care, truant youth). Interventions that seemed to be more broadly successful were delivered in school settings and involved students' families. Familias Unidas consists of 12 family-based sessions designed to improve family communication, develop positive parenting, and enhance parental monitoring to reduce risky substance use among Hispanic adolescents (E. O'Connor et al., 2020). Brief interventions in a primary care setting were found to be relatively ineffective at preventing substance use in young adults (Saitz et al., 2021).

Adolescent substance use is often identified in a primary care setting, where healthcare personnel may lack the training or skills to provide developmentally appropriate, evidence-based interventions (Hadland et al., 2021). Referrals often place young people in treatment settings more appropriate for adults. Because the SUD treatment system often focuses on adults, it can be hard to know where to refer adolescents for screening and assessment. Given the associations between risk-taking and substance use, adolescents with substance use problems often become involved in the juvenile justice system. The gaps in the SUD continuum of care for adolescents may help explain the difficulties in treating this population.



NIDA'S PRINCIPLES OF ADOLESCENT SUD TREATMENT

A NIDA (2014b) research-based guide sets out these 13 principles of adolescent SUD treatment:

1. Adolescent substance use needs to be identified and addressed as soon as possible.
2. Adolescents can benefit from a drug abuse intervention even if they are not addicted to a drug.
3. Routine annual medical visits are an opportunity to ask adolescents about drug use.
4. Legal interventions and sanctions or family pressure may play an important role in getting adolescents to enter, stay in, and complete treatment.
5. SUD treatment should be tailored to the unique needs of the adolescent.
6. Treatment should address the needs of the whole person, rather than just focusing on his or her drug use.
7. Behavioral therapies are effective in addressing adolescent drug use.
8. Families and the community are important aspects of treatment.
9. Effectively treating SUDs in adolescents requires also identifying and treating any other mental health conditions they may have.
10. Sensitive issues such as violence and child abuse or risk of suicide should be identified and addressed.
11. It is important to monitor drug use during treatment.
12. Staying in treatment for an adequate period of time and continuity of care afterward are important.
13. Testing for sexually transmitted diseases (e.g., HIV; hepatitis B and C) is important in drug treatment.

For more on each principle, see NIDA's *Principles of Adolescent Substance Use Disorder Treatment: A Research-Based Guide* (<https://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/principles-adolescent-substance-use-disorder-treatment>).

Behavioral treatments such as CM, CBT, and treatment regimens that mix the two approaches (e.g., the Matrix model) remain the best evidence-based treatments for stimulant use disorder (NIDA, 2019e).

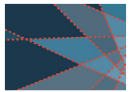
Because of their rapid cognitive development, adolescents are more adept than adults at incorporating new information and adapting their behavior to new social contexts (Davidow et al., 2016). This tendency supports the use of behavioral approaches and those that involve family members in treatment of adolescent SUDs (Silvers et al., 2019). Approaches that focus on parent training and family communication (e.g., Strengthening Families Program, Community Reinforcement and Family Training [CRAFT]) can enlist family members as a stabilizing influence on adolescents.

Peer-based SUD services may enhance other services such as screening, brief intervention, and referral to treatment (SBIRT) and help adolescents

with SUDs engage in treatment when other support services are not readily available in the community (Winn et al., 2019). Peer services may also be particularly important for engaging adolescents in mutual-help programs, like 12-Step groups (Nash, 2020). (A 2016 review of case series studies yielded promising, although not definitive, findings that active participation in mutual-help groups by adolescents with substance misuse increases the likelihood that they will achieve abstinence [Bekkering et al., 2016].)

Specifically, peer recovery support specialists can aid adolescents with SUDs by (Nash, 2020):

- Introducing them to sober activities.
- Helping orient them to the philosophies and benefits of 12-Step groups.
- Helping them resolve feelings of ambivalence or resistance to SUD treatment.
- Serving as positive role models of recovery.



People Experiencing Homelessness/Unstable Housing

Per the *2020 Annual Homeless Assessment Report to Congress*, approximately 580,000 Americans were homeless on any given night in 2020 (Department of Housing and Urban Development, 2021).

Some people experiencing homelessness or unstable housing also experience problems with stimulant use. Data from 12 SUD treatment programs in the National Drug Abuse Treatment Clinical Trials Network showed almost 32 percent of patients had unstable housing and nearly 6 percent were experiencing homelessness (Pan et al., 2020).

Compared with patients experiencing homelessness and those who were stably housed, patients with unstable housing had the highest prevalence of cocaine use (about 45%), opioid use (42%), and combination stimulant–opioid use (25%). In a primary care sample of people experiencing homelessness, 16 percent reported 3-month cocaine use (Stringfellow et al., 2016). The 2005–2015 Treatment Episode Data Sets show that, among people experiencing homelessness who entered SUD treatment, 13 percent reported cocaine as their primary substance and 8.5 percent reported MA (Famutimi & Thompson, 2018). People using injectable drugs and currently experiencing homelessness who were surveyed as part of the 2015 National HIV Behavioral Surveillance System had a high rate of injecting MA (almost 72%) or injecting both MA and heroin (77%) in the previous year (Al-Tayyib et al., 2017).

Adolescents and young adults who experience homelessness/unstable housing are also vulnerable to stimulant use. In a study of youth with a history of homelessness, nearly 22 percent reported using MA 20 times in the previous 30 days (Yoshioka-Maxwell et al., 2015). Additionally, a 2012–2013 survey of youth in California who were homeless revealed that nearly 11 percent misused prescription stimulants only, and about 21 percent misused both prescription stimulants and prescription sedatives (Rhoades et al., 2014).

The clinical picture of individuals who use stimulants and experience homelessness/unstable housing is difficult to characterize because of the diversity of challenges these individuals face. Such challenges can include one or more of the following (Cox et al., 2017; Nyamathi et al., 2012; Torchalla et al., 2011):

- Serious mental illness and other mental disorders
- Chronic health conditions
- A tendency toward injection drug use
- A history of trauma (e.g., being a victim of sexual violence)
- A history of emergency department visits
- An elevated risk of engaging in transactional/survival sex
- Elevated rates of infectious diseases, like HIV or hepatitis C virus (HCV)
- Elevated rates of polysubstance use (e.g., alcohol)

Clinicians should recognize that, in patients who are using MA or cocaine and engaging in transactional/survival sex, the stimulant use may allow them to engage in sex work that provides them with a source of income. Such patients may have ambivalence about abstaining from stimulants. Walls and Bell (2011) describe the use of transactional/survival sex as common among youth and young adults experiencing homelessness who also have SUDs, including stimulant use disorders (especially ones involving MA and crack cocaine). The association between transactional/survival sex and injection drug use is particularly strong.

Stimulant use can also serve a functional purpose when people are evicted from housing. Individuals who are newly homeless may initiate or return to MA use because they perceive this as helpful in coping with the demands and stressors of their situation (Damon et al., 2019). In qualitative interviews of women experiencing homelessness and using stimulants, some women reported that stimulant use helped them stay awake and alert to protect themselves from physical harm or theft (McKenna, 2013).

Rather than shaming or stigmatizing patients for engaging in functional stimulant use, clinicians should be empathetic and try to understand the extent to which people with homelessness/unstable housing sometimes engage in high-risk behaviors to protect themselves and survive.

When working with patients with stimulant use disorders who are homeless or housing insecure, clinicians should:

- Refer them to case managers who can help them navigate health and social support systems.
- Teach them harm reduction strategies (especially ones related to sex work and HIV prevention).
- Help connect them to available places to shower, use the toilet, and sleep.
- Link them with social services that can provide basic hygiene tools and health products—like soap, toothbrushes, toothpaste, condoms, and menstrual products—and, for patients who inject stimulants, soap and water or alcohol-based hand sanitizer or alcohol pads to cleanse the injection site and antibacterial ointment to heal injection sites.
- Consider using Housing First approaches to treatment initiation (Baxter et al., 2019). (For more information on Housing First, see <https://www.hudexchange.info/resource/3892/housing-first-in-permanent-supportive-housing-brief/>).

Given the unique challenges and complex issues facing people experiencing homelessness or unstable housing, such patients may benefit from referral to a peer recovery support specialist, if available. Peer support in this population has been associated with reduced drug and alcohol use and lower rates of return to substance use (Barker & Maguire, 2017). Other non-substance-related outcomes of value associated with peer support among people with homelessness/unstable housing include improvements in quality of life and in social support (e.g., increase in certain types of social support, decrease in loneliness), an increase in mental health functioning and a reduction in psychiatric symptoms, a decrease in number of days homeless and lower risk of returning to homelessness, a decrease in number of criminal arrests, and improvements in self-efficacy and self-esteem (Barker & Maguire, 2017).

Harm reduction and supportive services like these can be especially helpful for patients who have stimulant use that serves a functional purpose, because these individuals might be unwilling to abstain from cocaine or MA use.

For people who are interested in formal SUD treatment, CM (see Chapter 4 for more discussion) has demonstrated effectiveness in helping patients with homelessness/unstable housing and SUDs improve psychological and emotional distress, abstinence, and treatment retention (Fletcher et al., 2014; Rash et al., 2017). Supplementing CM with nurse-led case management is also associated with reduced drug use and reduced number of sexual partners among sexual minorities (e.g., gay, bisexual) experiencing homelessness and using stimulants (Nyamathi et al., 2017; Zhang et al., 2018).

For more guidance on providing SUD and mental health services for people who are homeless or experiencing unstable housing, see TIP 55, *Behavioral Health Services for People Who Are Homeless* (<https://store.samhsa.gov/product/TIP-55-Behavioral-Health-Services-for-People-Who-Are-Homeless/SMA15-4734>).

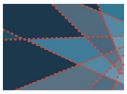
Rural Populations

According to 2010 census data, approximately 20 percent of the U.S. population lives in rural areas, with 704 counties or county statistical equivalents classified as completely rural and 1,185 counties or county statistical equivalents classified as mostly rural (Ratcliffe et al., 2016). Most of these counties are in Western states, where MA use is high.

Rural areas offer drug manufacturers and dealers secluded areas in which to produce illegal drugs, including MA; access to major routes for transporting illegal drugs to other regions for sale and distribution; and a customer base. Illegal drug manufacturers and dealers can often operate in rural areas with minimal risk of discovery because of fewer local law enforcement resources.

Prevalence in Rural Areas

MA has the highest availability in the Western and Midwestern United States, with more than 70 percent of local law enforcement agencies in these



areas identifying it as the greatest drug threat (NIDA, 2019d). In nonmetro areas, an estimated 8,000 adolescents ages 12 through 17 took part in past-year use of MA in 2019 (CBHSQ, 2020a). Similarly, an estimated 465,000 adults age 18 and older engaged in past-year use of MA in 2019 (CBHSQ, 2020a).

Rates of cocaine use in nonmetro areas were comparable to rates of MA use, with 10,000 adolescents ages 12 through 17 and an estimated 466,000 adults age 18 and older taking part in past-year use in 2019 (CBHSQ, 2020a).

Results from the 2019 NSDUH also showed that 48,000 adolescents ages 12 through 17 who were living in nonmetro areas engaged in past-year misuse of prescription stimulants (CBHSQ, 2020a). Further, 456,000 adults age 18 and older who were living in nonmetro areas engaged in past-year misuse of prescription stimulants (CBHSQ, 2020a).

Treatment admissions for MA are highest in Western states. Data from the National Drug Early Warning System suggest 12 to 29 percent of sites located west of the Mississippi River reported MA as the primary substance for treatment admission, compared with less than 1 percent of sites east of the Mississippi River (NIDA, 2019d).

In 2017, there were approximately 140,000 primary MA admissions among people age 12 and older in Western states, compared with approximately 13,000 primary cocaine admissions in the same group (CBHSQ, 2019). Primary MA admission rates rose consistently in Southern and Midwestern states between 2011 and 2017 (CBHSQ, 2019).

Challenges, Limitations, and Barriers to Treatment Services Faced by Rural Areas

Many rural areas have no specialized SUD treatment at all. Often, only one multiservice provider is available, and that provider can be overwhelmed by the area's various needs (L. B. Young et al., 2015). Additionally, rural areas have fewer formalized processes available to support and facilitate case management (Clary et al., 2020). Budget constraints limit SUD care, staff salaries (which contributes to high staff turnover), and the ability to provide support services such as

childcare or transportation. There are rarely any sources within the community from which to seek additional funding.

Lack of SUD treatment providers and lack of public transportation in rural areas make accessing specialty SUD care difficult for many rural patients (SAMHSA, 2016). Lack of privacy is another barrier to treatment. When a rural community has one or more SUD treatment providers, the comings and goings of patients can often be easily observed by people who know them (Clary et al., 2020; L. B. Young et al., 2015). This can contribute to concerns about stigma associated with seeking SUD services. Offering telehealth will not always overcome these barriers, as many rural households lack high-speed broadband Internet access (SAMHSA, 2021b).

Lack of access to medical services and insurance is a major barrier in providing evidence-based treatment services for people using stimulants. Advocacy for expanded Medicaid programs and coverage of evidence-based treatments like CM is necessary to adequately address the needs of rural populations (Clary et al., 2020; Cucciare et al., 2019).

Strategies To Provide Services in Rural Areas

Using the following strategies can help provide treatment services to rural populations:

- Partner with local agencies and stakeholders. Public safety and public health organizations can help create a coordinated response that streamlines the care of patients who use stimulants.
- Partner with public and private schools to provide information about prescription stimulant misuse in youth. This includes educating middle and high school students about the dangers of prescription stimulant misuse and strategies for coping with academic demands.
- Identify patients' nontreatment needs, provide temporary case management, and make referrals to case managers for ongoing support.
- Use telehealth to access experts who can provide specialty training for staff (e.g., Project ECHO; Browne et al., 2016; Zhou et al., 2016).

- Provide education about stimulant use disorders to local community members to raise awareness regarding treatment options.
- Increase access to treatment by using one or more medical vans to take SUD services and other care to rural communities (Gibson et al., 2014).
- Provide safe, substance-free living arrangements for patients who do not reside nearby. Funds can be specially designated, solicited through recovery community networking, or obtained through donations.
- Provide treatment services that are flexible in scope and structure (Browne et al., 2016; Timko et al., 2016). For example, an intensive outpatient (IOP) program might offer longer sessions on weekends instead of shorter, more frequent weekday sessions.
- Maximize patient engagement by assigning homework, arranging phone check-ins, having drug testing done by outlying clinics, using online communication, and holding weekend workshops or retreats.
- Use nontraditional sites and work arrangements to provide treatment services. If a treatment facility in a small rural community is not realistic, employ a part-time person who travels to satellite sites to provide outpatient services.
- Increase access to care via telemedicine and virtual visits (SAMHSA, 2016, 2021b). Additional research is needed to evaluate whether methods of access affect treatment outcomes for individuals with stimulant use disorders.
- Promote engagement in social–recreational activities beyond traditional mutual-help groups. Among rural people who use stimulants, increased engagement in social–recreational activities was associated with decreased substance use and decreased criminal recidivism (Timko et al., 2017).

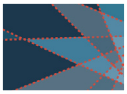
See this Rural Health Information Hub (<https://www.ruralhealthinfo.org/topics/substance-use>) webpage on substance use in rural areas for resources and more information.

People Involved in the Criminal Justice System

The number of people in state and federal prisons in the United States has been declining since its peak in 2008. Despite this decline, the United States still incarcerates a larger percentage of its population than any other country (Pew Research Center, 2020). According to the Department of Justice’s Bureau of Justice Statistics (BJS), 0.42 percent of U.S. residents—1.43 million people—were in state or federal prison in 2019 (Carson, 2020).

The rate of imprisonment for Blacks/African Americans is at its lowest since 1989, before laws passed during the “war on drugs” imposed stiff mandatory jail sentences for drug-related crimes (BJS, 2020). Since 2006, the imprisonment rate for Blacks/African Americans has dropped 34 percent. Over the same period, Hispanic and White Americans’ rates of imprisonment also dropped, by 26 and 17 percent, respectively. Even with the more rapid decline in their rates of incarceration, Blacks/African Americans are still imprisoned at a rate twice that of Hispanics and 5 times that of Whites (Pew Research Center, 2020).

Substance use and criminal justice involvement are highly correlated. The manufacture, possession, or sale of a variety of drugs are criminal offenses; thus, many people are in prison for committing drug-related crimes. Nearly 243,000 people nationwide are in state and federal prisons for drug offenses. As of May 2021, drug offenses accounted for almost half the inmates in federal prisons (46.3%, or more than 66,000 people; Federal Bureau of Prisons, 2021). In 2018, one in seven inmates in state prisons (14%, or more than 176,000 people) was serving time for a drug offense (Carson, 2020). About 21 percent of inmates in state prisons say they committed their crimes to obtain drugs or money to buy drugs (Bronson et al., 2017). Two out of every five state prison inmates committed their crimes while on drugs. One in 6 was taking crack/cocaine; 1 in 10 was taking other stimulants, including MA (Bronson et al., 2017). Stimulant-related offenses account for 75 percent of all federal drug crimes (CDC, 2019).



But beyond these connections, the link between substance use and criminal activity is correlational, not causal (Farabee, 2018). Precisely how many people in prison have SUDs is not known, but an estimated 65 percent of the prison population has an SUD (NIDA, 2020c). In some studies of limited prison populations, the figure is as high as 87 percent (Proctor et al., 2019). According to BJS statistics, the incidence of SUDs among state prisoners is 14 times higher than among the general population not involved with the criminal justice system. Among state prisoners, 34 percent regularly used cocaine/crack and 23 percent regularly used other stimulants, including MA, with regular use defined as once a week for a month (Bronson et al., 2017). A study of 200 inmates in county jails found that, according to criteria in the fifth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), 34 percent met criteria for stimulant use disorder, the most prevalent SUD among study participants (Proctor et al., 2019).

In 2018, fewer than one in four people in federal prison (about 23%) participated in SUD treatment (BJS, 2020). A large nationwide study found that 30 to 33 percent of people with criminal justice involvement in the previous year received treatment for SUDs (Saloner et al., 2016). For people who have been incarcerated, having cocaine use disorder was strongly associated with receiving SUD treatment, either during or after incarceration (J. Tsai & Gu, 2019). However, the researchers noted that despite the strong correlation, treatment usage rates were still low.

The relative lack of treatment for people in prison represents a missed opportunity. Many are experiencing an extended period during which they are not using drugs and have available time and a structured environment in which to undertake treatment, yet access to evidence-based treatments is limited. Treatment in prison often consists mainly of mutual-help groups like Alcoholics Anonymous and Narcotics Anonymous or psychoeducation (J. Tsai & Gu, 2019). Other therapeutic approaches available to prisoners include CM, therapeutic communities (TCs), CBT, motivational enhancement therapy, and counseling that includes vocational and life-skills instruction.

As with people who are not incarcerated, social support is a key aspect of SUD treatment for people in prison. Inmates who receive more visits and phone calls from family and friends and who are allowed furlough days are more likely to access treatment while incarcerated. Compared with Black/African American and Latino prisoners, Whites were more likely to receive such social support (Nowotny, 2015).

Social support can also be particularly meaningful and effective when it comes from a peer recovery support specialist with a lived experience of incarceration and recovery from SUDs (Barrenger et al., 2019). A review of peer-delivered support services for SUDs among incarcerated individuals found evidence that peer services were associated with an increase in 30-day abstinence rates before release from incarceration, a greater likelihood of completing SUD treatment once released, and a decrease in future criminal justice charges (Bassuk et al., 2016).

One example of how peer recovery support specialists can perform outreach in a criminal justice setting is providing recovery education to incarcerated individuals in the jail or prison. The incarcerated individual receives information about how to contact a peer recovery support specialist. Thirty days before release, the individual calls the peer recovery support specialist and they begin building a relationship. The peer recovery support specialist helps the individual get a head start on developing a recovery plan in preparation for returning to the community.

Cos and colleagues (2020) looked at the use of peer recovery support specialists in an integrated, primary-care-based SUD treatment program in which all patients had a history of arrest with or without conviction, incarceration, or other criminal justice system involvement. Participation in the program was associated with a decrease in the percentage of patients using substances in the past 30 days, a reduction in number of days using alcohol, an increase in patient engagement in medical services after program enrollment, an increase in school enrollment, and an increase in rates of employment (Cos et al., 2020).

Therapeutic approaches that have been successful in treating stimulant use disorder in general populations (e.g., CBT, CM) have also shown success among criminal justice-involved populations, but much research into SUD treatment among prison populations has focused on TCs. TCs require long-term residence and center on peer group processes to promote behavioral change, making them ideally suited for incarcerated populations. A meta-analysis of therapeutic approaches used to treat SUDs in prison populations found that TCs were most effective at reducing recidivism and drug use after prisoners were released (Mitchell et al., 2012).

Reentering society after imprisonment is a challenge for all prisoners. Those with SUDs face the additional challenge of being back in the environment in which they used substances. Research indicates that released prisoners who used MA and cocaine at the time they entered prison have higher rates of recidivism than other former inmates, with the exception of those with OUD (Cumming et al., 2020; Wimberly et al., 2018). Follow-up care, in the form of telephone monitoring and counseling, in addition to IOP treatment, has been shown to decrease the odds of people with cocaine dependence having a criminal conviction for 4 years following release from prison, when compared with those who had only IOP treatment (Wimberly et al., 2018).

Prisoners with stimulant use disorders who are reentering society should be referred to SUD care. Recovery support and other services they may benefit from include:

- Continued interaction with peer recovery support specialists.
- Connection to support services (e.g., reentry programs, vocational rehabilitation, transportation and housing assistance) in the community.
- Multidisciplinary case management services for medical and psychiatric care.

For more information on this topic, see these SAMHSA publications: *Principles of Community-based Behavioral Health Services for Justice-involved Individuals: A Research-based*

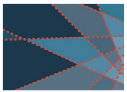
Guide (<https://store.samhsa.gov/product/Principles-of-Community-based-Behavioral-Health-Services-for-Justice-involved-Individuals-A-Research-based-Guide/SMA19-5097>); TIP 44, *Substance Abuse Treatment for Adults in the Criminal Justice System* (<https://store.samhsa.gov/product/TIP-44-Substance-Abuse-Treatment-for-Adults-in-the-Criminal-Justice-System/SMA13-4056>); and *After Incarceration: A Guide to Helping Women Reenter the Community* (<https://store.samhsa.gov/product/After-Incarceration-A-Guide-To-Helping-Women-Reenter-the-Community/PEP20-05-01-001>).

People Taking Medication for Opioid Use Disorder

People receiving OUD medication treatment may be prescribed one of the three Food and Drug Administration (FDA)-approved medications for OUD: methadone, buprenorphine, or naltrexone. All three may be offered by federally approved opioid treatment programs (OTPs). Buprenorphine treatment may be offered in other settings by healthcare professionals with the federal waiver required for prescribing buprenorphine, and naltrexone may be offered by any prescriber (SAMHSA, 2020h).

Cocaine is among the nonopioid substances most frequently used by people taking medication for OUD. It was present among 24 percent of patients in one study of more than 19,000 OTP admissions from 2011 to 2013 (Fong et al., 2015). In a trial of 177 patients being treated with buprenorphine, 26 percent screened positive for DSM-IV-defined cocaine abuse or dependence (APA, 2000; Schottenfeld et al., 2014). And among 791 pregnant women receiving methadone or buprenorphine, 21 percent had a history of cocaine use, whereas 1.4 percent had a history of amphetamine/MA use (Krans et al., 2016).

Among patients entering OTPs for OUD between 2012 and 2018, the prevalence of past-month MA use rose from almost 8 percent to about 21 percent (Severtson et al., 2019). In 799 patients taking buprenorphine through the SAMHSA-funded Washington State Medication Assisted Treatment–Prescription Drug and Opioid Addiction



(WA-MAT-PDOA) program clinic between 2015 and 2018, 30 percent reported past-month MA use and 15 percent past-month cocaine use (Tsui et al., 2020).

Clinicians treating patients for OUD should also make efforts to help patients stop or reduce any stimulant use. Regular cocaine use can decrease serum concentrations of methadone and buprenorphine and—in patients without HIV—may reduce peak concentrations of methadone (Tetrault et al., 2015). The potential effects of cocaine on the pharmacokinetics of opioid agonist therapy are important, because people taking opioid agonist medication and using cocaine at the same time may not experience the full clinical benefit of the medication, which could lead to poor treatment outcomes (Tetrault et al., 2015). Also of note, both cocaine and MA may increase the risk of cardiac arrhythmia in the presence of methadone. Therefore, patients with current or past stimulant use who are taking methadone for OUD should be assessed and monitored for risk of cardiac arrhythmias, specifically a risk for prolonged QT interval. (For more information, see TIP 63, *Medications for Opioid Use Disorder* [<https://store.samhsa.gov/product/TIP-63-Medications-for-Opioid-Use-Disorder-Full-Document/PEP20-02-01-006>]).

Some patients may report that methadone lengthens and mellows the effects of cocaine, presumably attenuating negative reinforcers associated with acute cocaine withdrawal. Patients taking buprenorphine or methadone for OUD who continue to use stimulants should not have their OUD medication stopped (American Society of Addiction Medicine, 2020). It is more appropriate to increase services and add adjuvant treatment, including CM, closer cardiac monitoring, and harm reduction education.

Longitudinal data are lacking on whether and how OUD medication might affect co-occurring stimulant and opioid use disorders (Rawson, 2020). In the case of cocaine use while on medication for OUD, findings thus far are mixed. In one study, cocaine use was associated with shortened duration of abstinence from opioids following methadone or buprenorphine/naloxone treatment (Zhu et al., 2018). But two other studies found no

effect of cocaine use on retention in buprenorphine treatment (C. O. Cunningham et al., 2013; Weinstein et al. 2017). Among OTP patients with baseline cocaine use who were randomized to either buprenorphine/naloxone or methadone, methadone was more effective at reducing number of days of opioid use, whereas the two medications were equally effective at reducing opioid use in patients without baseline cocaine use (Hser et al., 2016). Thus, in some OTP patients who have concurrent opioid and cocaine use, methadone might be more effective than buprenorphine/naloxone in helping them achieve abstinence from opioids, but it is unclear which OUD medication would definitively yield better results for patients with both opioid and stimulant use disorders.

Compared with cocaine, there appears to be less research about the effects of MA on opioid medication, but what data are available suggest a negative relationship. In the WA-MAT-PDOA study, people with past-month MA use were in buprenorphine treatment for a significantly shorter length of time and were more likely to drop out or be terminated from treatment within the first 3 months, compared with people who did not report past-month MA use (Tsui et al., 2020). Past-month MA use in the same study was associated with more than 2 times the relative risk for treatment nonretention than not having past-month MA use.

There appears to be very limited data from U.S. trials in humans on the effects of stimulants on naltrexone/extended-release naltrexone for OUD, making it hard to draw conclusions about whether cocaine and MA influence outcomes with these medications specifically. However, in some small samples, naltrexone has been associated with reduced cue-induced craving and subjective feelings of craving in people who use MA (Ray et al., 2015; Roche et al., 2017).

In a very small qualitative, exploratory study of 25 patients with current or recent stimulant use who were taking OUD medication, participants reported feeling that (Rawson, 2020):

- Stimulants seemed, subjectively, to be more “addicting” than opioids.
- Craving was a strong factor in their ambivalence about stopping stimulant use.

- Individual and group counseling was not helpful to their stopping stimulant use, but avoidance practices (e.g., not carrying cash, avoiding friends who use substances) were.

In addition, the few people in the study who had previously participated in CM for stimulant use reported finding it very helpful. (See Chapter 4 for more information about CM for stimulant use.)

Peer recovery support specialists can play a role in helping people with OUD access medication treatment. Samuels et al. (2019) trained recovery coaches (another term for peer recovery support specialist) from a community-based recovery organization to approach patients treated and discharged from an emergency department following opioid overdose. Recovery coaches were trained to assess overdose risk factors and readiness to seek treatment and to provide individualized support and linkage to providers who could prescribe medication for OUD. The median number of days before starting OUD medication was shorter among the people given access to a recovery coach, compared with people discharged as usual.

People Who Inject Drugs

Injecting cocaine or MA, like injecting other drugs, poses a major public health problem because of potential HIV and hepatitis transmission. This transmission can occur when people who inject cocaine or MA share infected injecting equipment. Transmission can also occur when PWID with HIV or hepatitis have sexual contact, especially unsafe contact, with others.

Prevalence of Injecting Drugs in People Who Use Stimulants

An estimated 6.6 million people age 13 and older, representing 2.6 percent of the U.S. population, had injected drugs, including stimulants, as of 2011 (Lansky et al., 2014). Among adults reporting past-year MA use between 2015 and 2018, 22.3 percent injected MA (C. M. Jones et al., 2020). Many PWID have unmet healthcare service needs and poorer long-term outcomes, like experiencing homelessness or incarceration (Dasgupta et al., 2020; Genberg et al., 2015; Linton et al., 2013; Robbins et al., 2010).

Pattern of Use and the Consequences

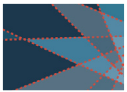
One factor that may increase risk of infection among PWID is their pattern of use. Cocaine is frequently used in intermittent cycles of repeated multiple uses known as binges (Vosburg et al., 2010). This pattern of use, observed in human laboratory studies (Foltin et al., 2015; Vosburg et al., 2010), often leads to more frequent injections during a binge than are generally observed in people with opioid use disorder.

This greater frequency of injection during a binge appears to have a greater likelihood of HIV infection. In a meta-analysis of global HIV risk among PWID (including in North America), the risk of HIV incidence was 3.6 times higher for people injecting cocaine and 3.0 times higher for people injecting amphetamine-type stimulants, compared with the risk for people who had not injected the drugs in the previous 6 months (Tavitian-Exley et al., 2015).

Data from CDC suggest that PWID are about 16 times more likely than people without injection drug use to develop invasive methicillin-resistant *Staphylococcus aureus* (staph) infections (Jackson et al., 2018). Another emerging medical issue related to injection drug use CDC has identified is infective endocarditis (an infection in the heart; CDC, n.d.-e). Injection drug use is the main cause of infective endocarditis. Anywhere from 5 to 10 percent of total deaths among PWID are due to this condition (Ji et al., 2012), which has an inpatient mortality rate of about 5 to 8 percent. The number of PWID younger than age 35 who died from infective endocarditis doubled from 1999 to 2016 (Kadri et al., 2019). *Staphylococcus aureus* causes between 52 and 62 percent of cases of infective endocarditis in PWID (See et al., 2020).

Reducing Injection Drug Use and Its Consequences

A variety of interventions have been used to prevent the initiation of injection drug use (for a review, see Werb et al., 2013) and reduce the consequences of injection drug use (for reviews, see Jeal et al., 2015; MacArthur et al., 2014). These interventions are tailored to PWID in general. Beyond promoting cessation of injection drug use



through comprehensive SUD care, it is important to educate PWID regarding harm reduction principles and safer injection practices to avoid the negative consequences of injection drug use.

Evidence shows that multicomponent HIV prevention programs—which provide antiretroviral medication, HIV testing, access to and education about condoms, and behavioral prevention skills training to people with HIV and their partners—reduce the risk of transmission over time (CDC, 2016).

Syringe access programs have been implemented in a wide variety of circumstances throughout the world (Des Jarlais et al., 2013; Nguyen et al., 2014). Research on syringe access programs show that they reduce the risk of HIV and hepatitis and do not lead to more injection drug use (Abdul-Quader et al., 2013; Bramson et al., 2015; CDC, n.d.-f). Furthermore, education on safer injection practices reduces the risk of skin and soft tissue infection among PWID (Baltes et al., 2020). To learn about recommendations and guidelines for safer injection practices (e.g., supplies, injection sites, injection processes), see the National Harm Reduction Coalition's *Getting Off Right: A Safety Manual for Injection Drug Users* (<https://harmreduction.org/issues/safer-drug-use/injection-safety-manual/>) and the Boston Public Health Commission's Access Harm Reduction Overdose Prevention and Education Program Participant Guide (<https://www.bphc.org/whatwedo/Recovery-Services/services-for-active-users/Documents/Client%20Manual%20FINAL.pdf>).

Although research supports the use of syringe access programs (Platt et al., 2017) and safer injection education (Des Jarlais, 2017), barriers exist to using them for HIV and hepatitis risk reduction. For example, a study of adults who inject heroin identified greater distance from syringe access programs, worries about potential arrest for possession of syringes, and lack of appropriate preparation (i.e., not having alcohol, alcohol wipes, or new syringes available) as barriers to use of sterile needles (Phillips, 2016). Further, perceived stigma from pharmacists and syringe access program staff can also affect engagement among PWID (Paquette et al., 2018; Rivera et al., 2014).

Prior to the implementation of syringe access programs, the 1995 report *Preventing HIV Transmission: The Role of Sterile Needles and Bleach*, produced by a panel organized by the National Research Council and the Institute of Medicine (IOM; now the National Academy of Medicine), states that bleach disinfection, when performed according to the guidelines provided by CDC and SAMHSA's Center for Substance Abuse Treatment, is useful in preventing HIV infection for PWID who share injecting equipment. The IOM report recommends that PWID be trained in effective procedures and more research be conducted to identify the simplest effective disinfection procedures. Bleach disinfection is recommended in situations where alternative, effective interventions (e.g., syringe exchange programs) are not available.

People Living With HIV/AIDS

People who use stimulants are at higher risk for HIV acquisition, as they are more likely to (SAMHSA, 2020j):

- Engage in condomless sex.
- Have multiple sexual partners.
- Reuse or share injection drug equipment.

People who inject stimulants may be at elevated risk for HIV acquisition compared with individuals who inject other substances, because of the frequency with which injection of stimulants occurs (Tavitian-Exley et al. 2015). Sexual activity, in particular being an anal receptive partner, and needle sharing are common routes of HIV acquisition for people who inject stimulants. Exhibit 6.2 lists the probabilities of acquiring HIV from an infected source for various types of exposure. Providers need to address risk factors for HIV transmission with patients using stimulants.

EXHIBIT 6.2. Estimated Per-Act Probability of Acquiring HIV From an Infected Source by Exposure Act*

TYPE OF EXPOSURE	RISK PER 10,000 EXPOSURES
PARENTERAL (I.E., NONORAL)	
Blood Transfusion	9,250
Needle-Sharing During Injection Drug Use	63
Percutaneous (Needle-Stick)	23
SEXUAL	
Receptive Anal Intercourse	138
Insertive Anal Intercourse	11
Receptive Penile–Vaginal Intercourse	8
Insertive Penile–Vaginal Intercourse	4
Receptive Oral Intercourse	Low
Insertive Oral Intercourse	Low
OTHER†	
Biting	Negligible
Spitting	Negligible
Throwing Body Fluids (Including Semen or Saliva)	Negligible
Sharing Sex Toys	Negligible

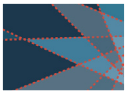
*Factors that may increase the risk of HIV transmission include sexually transmitted diseases, acute and late-stage HIV infection, and high viral load. Factors that may decrease the risk include condom use, male circumcision, antiretroviral treatment, and PrEP. None of these factors are accounted for in the estimates presented in the table.

†HIV transmission through these exposure routes is technically possible but unlikely and not well documented.

Sources:

- Patel, P., Borkowf, C. B., Brooks, J. T., Lasry, A., Lansky, A., & Mermin, J. (2014). Estimating per-act HIV transmission risk: A systematic review. *AIDS (London, England)*, 28(10), 1509–1519.
- Pretty, L. A., Anderson, G. S., & Sweet, D. J. (1999). Human bites and the risk of human immunodeficiency virus transmission. *American Journal of Forensic Medicine and Pathology*, 20(3), 232–239.

Source: Adapted from CDC (n.d.-b). Estimated per-act probability of acquiring HIV from an infected source, by exposure act (<https://www.cdc.gov/hiv/risk/estimates/riskbehaviors.html>).



Screening people with stimulant use disorders for HIV should be part of the standard of care provided by SUD treatment programs (SAMHSA, 2020j). Patients may be reluctant to undergo an HIV test because they fear the results or because of stigma related to HIV/AIDS. Clinicians can help to increase both HIV testing uptake and engagement among patients who have a positive test by educating patients about effective treatments for HIV and the concept of “undetectable equals untransmittable” (U=U). The U=U slogan, which is part of the Prevention Access Campaign, conveys to patients that they cannot transmit HIV sexually if they are adherent to antiretroviral therapy (ART) and they do not have detectable levels of HIV in their blood for at least 6 months (Eisinger et al., 2019). In the setting of highly active antiretrovirals, a durably suppressed HIV viral load truly is treatment as prevention.

Many factors may delay a diagnosis of HIV in patients who use stimulants and it is more likely that patients using stimulants will have an AIDS diagnosis at the time of their positive HIV test (United Nations Office on Drugs and Crime, 2019a). Patients living with HIV and using stimulants may have increased risk for progression to an AIDS diagnosis and increased all-cause mortality (Carrico et al., 2014).

For patients who have a positive HIV screen, clinicians should confirm the diagnosis and link the patients to HIV care immediately for evaluation by a treatment provider (SAMHSA, 2020j). This may be overwhelming for patients, particularly in the setting of active substance use. Clinicians can avoid delays in linkage to care and promote patient safety by using a warm-handoff approach, in which the patient’s care is transferred between providers in the presence of the patient.

Treating people living with HIV/AIDS (PLWHA) is another area in which program linkages become critical to successful treatment. It is helpful, where possible, to have medical staff skilled in both HIV and SUD care to provide patients convenient access to treatment for both chronic health conditions. Given the complex stigma patients face when living with HIV and SUD, it is imperative to seamlessly transition patients and refer them to appropriate care providers.

Although ART has advanced significantly and new medication regimens like long-acting injectable products are on the horizon, daily medication adherence is still pivotal to having a durably suppressed viral load. In patients injecting stimulants, daily ART adherence is affected. Stimulant use is correlated with lower daily adherence, but does not necessarily correlate with increased levels of detectable HIV viral loads (Marquez et al., 2009). Additional research has found that positive affect intervention coupled with community-based CM may be effective in increasing viral suppression and limiting patients’ stimulant use (Carrico, Hunt, et al., 2019; Carrico, Neilands, et al., 2019).

MA has been associated globally not only with higher rates of HIV acquisition, but also with more difficulty in patients reaching HIV viral suppression (Mastro et al., 2020). Among people who use MA and are living with HIV, there is an increased likelihood of transmitted drug resistance (Cachay et al., 2007). Multiple mechanisms of action have been indicated for the worsening outcomes for PLWHA and using MA, including inflammation (Castillo-Mancilla et al., 2016), increased viral replication (Mastro et al., 2020), and immunologic dysfunction (Carrico et al., 2018) related to substance use.

One of the critical aspects of providing SUD treatment to PLWHA is the continuing education that clinicians need regarding the changing and complex array of medication regimens available to this population. Further, clinicians need an awareness of the compounded stigma that many PLWHA who use stimulants may face in seeking treatment in traditional medical systems (Brinkley-Rubinstein, 2015; Pescosolido & Martin, 2015).

Peer support may be crucial in helping PLWHA feel understood, encouraged, and supported in their recovery journey. In addition to facing SUDs, PLWHA may also be dealing with mental health issues and trauma, all of which make the recovery process particularly complex. Support from a peer can be powerful because of their understanding of:

- The complexities of living with HIV/AIDS.
- Accompanying substance-related, mental, and social needs.
- Ways to access needed resources.

For more information on this topic, see SAMHSA's publication *Prevention and Treatment of HIV Among People Living with Substance Use and/or Mental Disorders* (<https://store.samhsa.gov/product/Prevention-and-Treatment-of-HIV-Among-People-Living-with-Substance-Use-and-or-Mental-Disorders/PEP20-06-03-001>).

People With or At Risk for Hepatitis

Hepatitis is an inflammation of the liver. It is often caused by viruses, the most common of which in the United States are hepatitis A virus (HAV), hepatitis B virus (HBV), and HCV. HCV is the most prevalent hepatitis virus in the United States (CDC, 2021d). The primary mode of HCV transmission is injection drug use, particularly among young adults and rural populations (Harris et al., 2016; Iqbal et al., 2015; Page et al., 2013). Sexual contact is another common mode of transmission, particularly among PWID with sexual behavior with an elevated risk of tissue tearing (Tracy et al., 2014) or with co-occurring HIV infection (J. Chen et al., 2014).

The prevalence of lifetime HCV infection among PWID ranges from 65 to 90 percent (Crawford & Bath, 2013; P. K. Nelson et al., 2011). HCV seropositivity is correlated with duration and frequency of injection (CDC, 2011). Among PWID who are also MSM and have HIV infection, the prevalence of detectable HCV infection is 40 percent (Jordan et al., 2017).

In a study of individuals who reported lifetime use of MA and who had susceptibility to HBV, 6.95 percent had active HCV infection (Tressler et al., 2020). People who use both MA and opioids have been shown to be almost twice as likely to have HBV or HCV compared with individuals who use opioids alone (Shearer et al., 2020). Another study found that among individuals who reported lifetime use of cocaine, 22 percent reported a history of HCV and 8 percent reported a history of HBV (Novick et al., 2016).

HCV begins as an acute infection but may become chronic, which can lead to liver disease, other serious health consequences, and death (SAMHSA, 2015). It is important to educate patients on the

symptoms of acute HCV infection to increase the likelihood of screening and healthcare-seeking behaviors. One of the biggest barriers to medical treatment for HCV is that 65 to 75 percent of people with chronic HCV infection are unaware of their status because they are asymptomatic and likely will be until the disease advances (McGowan & Fried, 2012). It is also apparent from in vitro studies and animal data that stimulant use may promote HCV replication and in turn increase disease progression (Ye et al., 2008).

Although no vaccine exists for HCV, effective and well-tolerated medications that can cure HCV are now available. The SIMPLIFY study demonstrated that stimulant use negatively impacts adherence to directly acting antivirals. However, the same study indicated that despite the issues with adherence related to stimulant use, patients continue to experience a functional cure with the completion of the therapeutic regimen (E. B. Cunningham et al., 2018).

Vaccines for HAV and HBV have existed for years (CDC, 2015), although HBV vaccination coverage among adults remains low, especially among PWID (Harris et al., 2016). Despite the availability of HAV and HBV vaccines, outbreaks of these infections have occurred in many states in the past decade. HBV outbreaks have been attributed in large part to injection drug use, and people who use drugs. Additionally, PWID are at increased risk for HAV, which is foodborne (CDC, 2021c; Foster et al., 2019; Iqbal et al., 2015).

SUD care providers can make a major contribution to public health, as well as their patients' health, by screening for viral hepatitis or assisting patients in getting such screening. Exhibit 6.3 describes hepatitis risk and prevention for people who use stimulants. The U.S. Preventive Services Task Force (USPSTF) recommends screening for HBV in adolescents and adults at increased risk for infection, which includes PWID (USPSTF, 2020b). The USPSTF recommends HCV screening at least once for all adults, but periodically for people at continued risk for HCV, which includes PWID (USPSTF, 2020a). SUD care for people with stimulant use or at risk for stimulant use ideally should include a screening for viral hepatitis in the initial assessment.

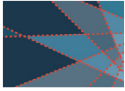
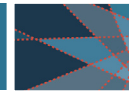


EXHIBIT 6.3. Hepatitis Risk and Prevention for People Who Use Stimulants

VIRUS	TRANSMISSION ROUTE	WHY PEOPLE WHO USE STIMULANTS ARE AT RISK	PREVENTION STRATEGIES
HAV	Fecal-oral	<p>MSM and people who use drugs have an increased risk for HAV infection (CDC, n.d.-c).</p> <p>Patients who use stimulants may be experiencing homelessness/unstable housing or otherwise are living in situations that are not adequate for hygienically preparing food. This is a risk factor because the virus can be contracted through HAV-contaminated food and water (CDC, 2020b).</p>	<p>Encourage patients to get their HAV vaccination (N. P. Nelson et al., 2020).</p> <p>Help patients with any personal hygiene needs and food preparation assistance (e.g., education about the dangers of eating uncooked food and how that might lead to HAV transmission; N. P. Nelson et al., 2020).</p>
HBV	Blood and body fluids	<p>Condomless sex with a partner living with HBV increases the odds of HBV transmission, particularly in the setting of dry mucosa and tissue tearing secondary to stimulant use.</p>	<p>Encourage patients to get their HBV vaccination (Schillie et al., 2018).</p> <p>Offer patients access to condoms for anal and vaginal intercourse.</p>
HCV	Blood-blood	<p>People who use stimulants may be injecting them, and injection drug use (including syringe sharing) increases the risk of HCV transmission among people using stimulants (Farrell et al., 2019).</p> <p>Stimulants can dry out body mucosa, increasing the risk for tissue tearing and transmission of HCV during sexual activities.</p> <p>People smoking or insufflating (i.e., snorting or inhaling) stimulants may share pipes or stems and have cracked lips, which could be a potential source of blood-blood transmission.</p> <p>People injecting stimulants may inject multiple times during a binge and may share injection equipment with others who are using injection drugs.</p>	<p>Offer patients treatments and services to help them stop injecting drugs (Office of Infectious Disease and HIV/AIDS Policy [OIDP], n.d.-b).</p> <p>Psychosocial treatments to stop stimulant use altogether also should be offered (Farrell et al., 2019).</p> <p>Teach patients about how to access and use safer injection equipment, and offer education about safer injection practices (Farrell et al., 2019; OIDP, n.d.-b).</p> <p>Educate patients about and encourage patients to practice safer sex while using stimulants (Farrell et al., 2019; OIDP, n.d.-b.). Offer patients access to condoms and lubrication for vaginal and anal sex.</p>



Providers who conduct these screenings need to recognize that individuals may hesitate to answer questions about injection drug use, sexual history, or potential risk for hepatitis because of mistrust, stigma, and discrimination. Further, hepatitis infection may be misattributed to sexual contact among PWID who provide accurate responses about their sexual practices but do not admit to injection drug use (Klevens et al., 2012), putting them at future risk for reinfection if they do not receive SUD treatment or harm reduction education.

SAMHSA's Hepatitis C Screening in the Behavioral Healthcare Setting Advisory (<https://store.samhsa.gov/product/Advisory-Hepatitis-C-Screening-in-the-Behavioral-Healthcare-Setting/sma15-4917>) provides an overview of how and why to conduct or make referrals for HCV screening, and also looks at the ways HAV, HBV, and HCV are transmitted. For additional information and resources, see the CDC Viral Hepatitis webpage (<https://www.cdc.gov/hepatitis/index.htm>).

Clinicians should also integrate education on hepatitis into SUD care. Education should include information, as appropriate, about the health benefits of:

- Participating in syringe services programs.
- Using protection when engaging in sex.
- Getting vaccinated against HAV and HBV.
- Taking medication for HCV.

SAMHSA's comic book-style publication *Take Action Against Hepatitis C: For People in Recovery From Mental Illness or Addiction* (<https://store.samhsa.gov/product/Take-Action-Against-Hepatitis-C/sma14-4853>) provides information directed to patients.

Individuals With Co-Occurring Mental Disorders

A patient with CODs has a combination of two or more SUDs and mental disorders as defined in DSM-5 (SAMHSA, 2020). Although a stimulant use disorder can coexist with any mental disorder, this section focuses on some of the mental disorders that are most often diagnosed in people with

a stimulant use disorder: depressive disorders, bipolar disorder, anxiety disorders, PTSD, ADHD, and schizophrenia.

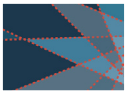
Someone who displays symptoms consistent with a mental disorder does not necessarily have an organic mental disorder but may have a substance-induced disorder or symptoms mimicking an organic mental disorder (per DSM-5). For example, people in withdrawal from stimulant use may show symptoms of depression, but they do not necessarily have a depressive disorder. Similarly, people who use MA may exhibit psychotic symptoms like those common in people with schizophrenia, but the psychotic symptoms are not conclusive evidence of schizophrenia and may resolve with cessation of substance use.

Other symptom clusters commonly associated with specific mental disorders are also frequently seen during the use of stimulants or during early abstinence. These symptom clusters include physical and psychological signs of anxiety, mood fluctuations, and antisocial behavior.

Some people with stimulant use seek psychiatric care for symptoms related to their stimulant use before entering SUD treatment. Some patients may use substances to treat symptoms of their organic mental illness rather than seeking formal treatment. In both cases, stigma about mental health concerns and SUDs can make people reluctant to engage in care (Zwick et al., 2020), which can result in a delayed diagnosis and ineffective treatment plans for individuals with co-occurring stimulant use disorder and mental illness (National Academies of Sciences, Engineering, and Medicine, 2016).

Someone with stimulant use who has previously received a psychiatric diagnosis or has symptoms typically associated with a mental disorder does not necessarily have CODs. Having CODs means both an SUD and a mental disorder are actively present, and the patient meets full criteria (rather than just symptoms) for both disorders.

The accurate diagnosis of mental illness in an individual with stimulant use requires considerable diagnostic skill on the part of the mental health service provider (Warden et al., 2016). It is often necessary to make a provisional diagnosis, which



is modified after additional data are collected. Additionally, for patients using stimulants like cocaine or MA, it is important to differentiate symptoms associated with an organic mental illness and symptoms of protracted withdrawal. For example, patients may have symptoms of depression and psychosis that accompany acute withdrawal symptoms, but they typically resolve within 1 week (Zorick et al., 2010).

Another important element in the diagnosis of a co-occurring mental disorder is obtaining a careful history of the chronological relationship between the onset of psychiatric symptoms and the substance use history. An accurate chronology can help clinicians determine whether there is a co-occurring mental disorder or the psychiatric symptoms are induced by the substance.

Clinicians should assess whether the outpatient setting is appropriate for evaluation of symptoms. Hospital admission allows for a more thorough evaluation of symptoms and factors that may contribute to the symptoms. Additionally, patients can be observed for resolution of particularly concerning symptoms, such as suicidal or homicidal ideation or psychotic symptoms that may affect individual or community safety (Kampman & Jarvais, 2015).

Given the many challenges people with CODs face, linking them with peer recovery support specialists may be beneficial. In one study, a treatment group of people with SUDs and co-occurring serious mental illness who participated in a peer support program spent more time living in the community before needing rehospitalization and had fewer rehospitalizations overall than did a comparison group without program participation (Min et al., 2007). Helping patients with CODs connect with peer recovery support specialists (including mutual-help programs devoted to CODs) should be a part of discharge planning, continuous care, and may even be combined with ongoing clinical interventions (e.g., CBT, medication treatment) to maximize positive outcomes (SAMHSA, 2020l).

Mutual-help programs for people with CODs—often called dual recovery mutual-help programs—are available to help patients find direction and support for recovery from both

mental illness and SUDs. More information about accessing dual recovery mutual-help programs can be found in SAMHSA's TIP 42, *Substance Use Disorder Treatment for People With Co-Occurring Disorders* (<https://store.samhsa.gov/product/tip-42-substance-use-treatment-persons-co-occurring-disorders/PEP20-02-01-004>).

Specialized Treatment Interventions

Depressive disorders

Past-year major depressive disorder occurs in about 10 percent of U.S. adults (Hasin et al., 2018). Major depression appears to be about 1.5 times more prevalent in women than in men (Hasin et al., 2018). Persistent depressive disorder (previously called dysthymia) is likely much less common, although current U.S. prevalence rates are unclear at this time. Data based on diagnostic criteria from DSM-IV show a 12-month persistent depressive disorder prevalence of 1.5 percent in U.S. adults (Blanco et al., 2010). Co-occurring persistent depressive disorder and episodes of major depressive disorder, known as “double depression,” have been shown to occur in 14 percent of patients who seek treatment for SUDs (N. Diaz et al., 2012). In a sample of patients with any stimulant use disorder who were receiving residential treatment, 22.6 and 9.4 percent met diagnostic criteria for major depressive disorder and persistent depressive disorder, respectively (Warden et al., 2016).

To screen for depressive disorders, clinicians can use an evidence-based screener such as the Patient Health Questionnaire (PHQ-9; Beard et al., 2016; Bentley et al., 2021).

Key recommendations for clinicians working with patients who have co-occurring depressive disorders include (SAMHSA, 2020l):

- Initiating medications as soon as patients engage in care (if feasible). It should be noted that for patients taking medications affecting serotonin (e.g., selective serotonin reuptake inhibitors), there may be an elevated risk for serotonin syndrome in the setting of continued

stimulant use. Patients should be educated about these signs and symptoms and advised on what to do should they experience them (Cooper & Sejnowski, 2013; Moss et al., 2019).

- Using integrated CBT approaches that draw on functional analysis of the relationship between depression and substance use, incorporate cognitive training, and encourage behavioral activation.
- Evaluating for the development of “double depression”—the occurrence of persistent depressive disorder and intermittent major depressive episodes.
- Evaluating whether antidepressant medication is warranted for managing depressive symptoms or providing a referral for a medication evaluation.
- Considering the temporal relationship between depression and SUD, which can be unclear and can affect treatment planning. Clinicians can avoid making assumptions about what is causing and maintaining depression or an SUD by using various treatment approaches that address both CODs.

Bipolar disorder

About 2 percent of U.S. adults report a lifetime history of bipolar disorder (Blanco et al., 2017). Results from the National Epidemiologic Survey on Alcohol and Related Conditions–III, a large epidemiological study using DSM-5 criteria, show a strong positive association between past-year drug use disorder (i.e., an SUD excluding alcohol) and bipolar I disorder, with an odds ratio of 1.5 (B. F. Grant et al., 2016). Patients with SUDs and bipolar disorder have an increased risk for an unstable and more severe course of illness, violence, and suicide (Swann, 2010). A co-occurring bipolar disorder and SUD is also associated with worse clinical outcomes compared with clinical outcomes for bipolar disorder alone (Farren et al., 2012).

Patients with bipolar disorder may use stimulants to self-treat depressive episodes. Additionally, given the elevated mood associated with stimulant use, it is not uncommon for patients using stimulants to experience manic symptoms while acutely intoxicated from stimulant use. Patients with bipolar disorder that is well managed by medication can be treated in traditional treatment

settings. Therefore, medication management, specifically daily adherence, is one of the most important issues in treating patients with bipolar disorder (Salloum & Brown, 2017).

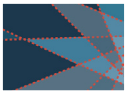
Anxiety disorders

In 2019, one in six (15.6%) adults age 18 and older reported experiencing symptoms of mild, moderate, or severe generalized anxiety within the past 2 weeks (Terlizzi & Villarroel, 2020). Nearly 7 percent of U.S. adults report having had panic disorder in their lifetime (Kessler et al., 2012). Patients with anxiety disorders and SUDs have greater symptom severity, more functional impairment, and poorer course of illness than patients with only an anxiety disorder or an SUD (Magidson et al. 2012; McHugh, 2015). In a sample of patients with any stimulant use disorder who were receiving residential treatment, 29.6 percent met diagnostic criteria for a co-occurring anxiety disorder, with generalized anxiety disorder (15.3%) and social phobia (10.6%) comprising the most common anxiety disorders (Warden et al., 2016).

To screen for generalized anxiety, clinicians can use an evidence-based screener such as the Generalized Anxiety Disorder scale (GAD-7; Bentley et al., 2021; Rutter & Brown, 2017).

Key recommendations for clinicians working with patients who have co-occurring anxiety disorders include (SAMHSA, 2020l):

- Identifying patients with elevated anxiety early in SUD treatment, which can help address risks that contribute to treatment engagement and retention as well as posttreatment relapse.
- Screening for elevated anxiety early in treatment to identify patients who may need additional skills to help them manage elevated distress related to stopping or decreasing their substance use.
- Discussing reasons for treatment concerns when relevant, especially adherence interference from anxiety symptoms or anxiety-related avoidance.
- Integrating a holistic approach to treatment, such as:
 - Providing psychoeducation about the nature of anxiety and its role in SUDs.



- Teaching CBT techniques to recognize and manage symptoms of anxiety.
- Discussing appropriate medication options, using motivational enhancement strategies.
- Practicing mindfulness techniques.
- Encouraging healthy lifestyle activities (e.g., diet, physical activity, sleep hygiene).
- Exercising extreme care in prescribing benzodiazepines for anxiety disorders, because of their high addiction potential.

Posttraumatic stress disorder

A strong association exists between PTSD and SUDs (B. F. Grant et al., 2015; B. F. Grant et al., 2016; Hasin & Kilcoyne, 2012). The lifetime prevalence of PTSD in people with SUDs is thought to range between 26 and 52 percent, and rates of current PTSD between 15 and 42 percent (Vujanovic et al., 2016).

People in treatment for a cocaine use disorder have double the odds of probable PTSD compared with people without cocaine use disorder, and the risk is greater for women than for men (Saunders et al., 2015). Among people who complete treatment for MA use disorder, PTSD is associated with more than 5 times greater odds of posttreatment MA use than not having PTSD (Glasner-Edwards et al., 2013). Women who are likely to experience trauma, such as those with current or past experiences of domestic violence, sexual assault, or homelessness, may be vulnerable to MA use and the negative effects of MA (Kittirattanapaiboon et al., 2017).

Clinicians need to obtain specialized training to work with individuals who have co-occurring SUD and PTSD. To screen for PTSD, clinicians can use an evidence-based screener such as the PTSD Checklist for DSM-5 (PCL-5; Blevins et al., 2015; Keane et al., 2014; LeardMann et al., 2021). Specialized treatment issues include relapse triggers, timing of addressing issues in group sessions, and the tools and social skills necessary to facilitate a successful recovery. Trauma-informed care should be universal throughout treatment settings. Learn more about how to provide trauma-informed care for patients with stimulant use disorders in SAMHSA's TIP 57, *Trauma-Informed Care in Behavioral Health Services* (<https://store.samhsa.gov/product/TIP-57-Trauma->

[Informed-Care-in-Behavioral-Health-Services/SMA14-4816](https://store.samhsa.gov/product/TIP-57-Trauma-Informed-Care-in-Behavioral-Health-Services/SMA14-4816)).

Key recommendations for clinicians working with patients who have co-occurring PTSD include:

- Acknowledging that disclosure is not the initial goal. Use a trauma-informed approach to help patients view the SUD care setting as a safe place at the beginning of treatment by using grounding exercises, treatment routines, safety-promoting behaviors, and safety plans. Be careful not to rush patients into discussing trauma and monitor the intensity and speed of the treatment for signs that patients are feeling overwhelmed (SAMHSA, 2020l).
- Treating PTSD and stimulant use disorder concurrently, as PTSD symptoms can worsen during abstinence (SAMHSA, 2020l).
- Implementing strategies to prevent retraumatization of patients, such as recognizing triggers and their cues, reacting to behaviors resulting from triggers in a sensitive manner, and teaching patients to identify and manage triggers (SAMHSA, 2020l).
- Recognizing the cyclical relationship between trauma and substance use and providing education to patients about this relationship. Having an increased awareness of this relationship allows patients to develop and implement safeguards (SAMHSA, 2020l).
- Referring patients to sexual assault and incest support groups as quickly as possible, as appropriate.
- Offering group counseling in a gender-responsive format that includes coaching on what to expect from dreams, fears, and sleep disruptions as a result of PTSD and withdrawal from stimulants.
- Providing information on practical tools to combat nightmares and sleep disruption—such as exercise, night lights, herbal teas, and relaxation techniques—as well as information on relapse triggers (McHugh et al., 2014). Such information will help provide patients with reassurance and skills to get through this period.
- Tailoring treatment to unique trauma-related symptoms and needs; the widely used Seeking Safety program is an example of such an approach (Berenz & Coffey, 2012; Lenz et al., 2016; Ruglass et al., 2014).

- Evaluating whether medication is warranted for managing PTSD symptoms or providing a referral for a medication evaluation (Berenz & Coffey, 2012).

Attention deficit hyperactivity disorder

The prevalence of ADHD is estimated to be 9.4 percent in children ages 2 to 17 (Danielson et al., 2018). The prevalence of adult ADHD is about 2.5 percent (Katzman et al., 2017). The co-occurrence of SUDs in people with ADHD is quite high, especially for cocaine, alcohol, nicotine, and cannabis (Klassen et al., 2012). Use of prescribed stimulant medication for children with ADHD is not associated with an increased risk of developing an SUD later in life (Klassen et al., 2012). Increasing numbers of young adults with ADHD are attending college, many of whom may be prescribed a prescription stimulant (Weyandt et al., 2013).

Clinicians need to retrieve a clear longitudinal history of both substance use and symptoms of ADHD before formalizing SUD and ADHD diagnoses. Symptoms of stimulant withdrawal or intoxication can mirror some symptoms of ADHD (e.g., impulsivity, attention difficulties, restlessness, agitation; Kaye et al., 2013). However, stimulant-related symptoms tend to disappear with time (when the patient is no longer in withdrawal or intoxicated).

Generally, adults with ADHD also had the disorder when they were children (that is, new onset usually does not occur in adulthood), although it may not have been diagnosed as such (Ahmad et al., 2019). An assessment of childhood symptoms should be part of completing the patient's history. The presence of ADHD symptoms in childhood provides a reliability measure for the presence of the adult disorder.

HOW TO TREAT ADHD IN PEOPLE WITH CO-OCCURRING STIMULANT USE DISORDER

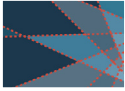
Stimulant medications are widely used, highly efficacious, and very effective for treating ADHD in children and adults. How can providers in primary care and integrated care settings approach ADHD management for adults who have co-occurring stimulant use disorder and want to pursue abstinence?

Not much research has been done on how best to treat patients with ADHD and co-occurring stimulant use disorder. The available studies have mixed findings on treatment effectiveness (J. Cook et al., 2017). High-dose stimulant medication has been suggested as a potential aid in reducing both ADHD and illicit stimulant use (J. Cook et al., 2017), with robust research support among people who use cocaine (Levin et al., 2015). This strategy would have to be used with diversion prevention and compliance/monitoring approaches, such as (Colaneri et al., 2017):

- Prescribing long-acting, rather than short-acting, stimulant formulations.
- Using medication contracts.
- Limiting prescriptions to a smaller number of pills.
- Implementing pill counts.
- Providing education about medications to patients.

For patients who want to be completely abstinent from all stimulants, several safe and effective nonstimulant ADHD medications with low addiction potential are available, such as atomoxetine, guanfacine, and clonidine (Clemow & Walker, 2014). Although not approved by FDA for the treatment of ADHD, antidepressants like venlafaxine and bupropion have also shown some use in reducing some ADHD symptoms (Katzman et al., 2017). However, nonstimulant medication is not considered a first-line pharmacotherapy for ADHD (Katzman et al., 2017). Pharmacotherapy should always be monitored closely for potential interactions with other drugs, side effects, or misuse, especially when prescribed to individuals with a history of SUDs.

Continued on next page



Continued

Several nonpharmacologic treatments for ADHD have demonstrated efficacy and should be a core part of any ADHD treatment plan, regardless of whether medication is also prescribed. In patients with stimulant use disorder who want to remain abstinent, reliance on nonpharmacologic interventions becomes even more critical. Such interventions are (Katzman et al., 2017):

- Psychoeducation (e.g., learning organizational skills, finding resources and support groups).
- Psychotherapy (e.g., CBT, interpersonal therapy).
- Behavioral interventions (e.g., teaching patients how to manage their environment, helping patients make healthy lifestyle changes, such as getting more exercise or better sleep).
- Social interventions (e.g., social skills training, anger management).
- School/workplace accommodations (e.g., being given extra time to complete tests, being allowed to close one's office door to minimize distractions).

Both conditions can be treated concurrently, but if the patient is destabilized because of stimulant use, the provider may need to address the SUD and stabilize the patient before pursuing ADHD treatment (Katzman et al., 2017).

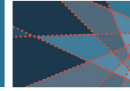
Schizophrenia

Schizophrenia is very uncommon in the United States, with somewhere between 0.3 and 0.7 percent of U.S. adults developing the disorder in their lifetime (APA, 2013). The prevalence of SUDs among people with schizophrenia is estimated to be as high as 55 percent (Kerner, 2015).

Key recommendations for clinicians working with patients who have co-occurring schizophrenia include:

- Treating SUD immediately to allow time for the medication for the mental illness to take effect. Both conditions should be treated at once, as substance use in schizophrenia can worsen disease course and may reduce adherence to antipsychotic medication (Werner & Covenas, 2017).
- Providing psychoeducation about schizophrenia, medication, and the importance of medication adherence for symptom control (SAMHSA, 2020l).
- Beginning treatment with deescalation and treatment of the psychotic symptoms through sleep, medications, and nutritional support. This is recommended because continuous cocaine or MA use, particularly in the setting of sleep deprivation, may result in psychotic symptoms and in severe cases may be completely indistinguishable from paranoid schizophrenia (J. M. Wilkerson et al., 2018).
- Providing treatment for both schizophrenia and stimulant use disorder with slight modifications after a stabilization period.
- Teaching patients to detect early signs of relapse for both schizophrenia and stimulant use or prescription stimulant misuse (SAMHSA, 2020l).
- Teaching patients to manage positive and negative symptoms of psychosis, increase coping skills, improve social skills (e.g., communication with others), expand social networks, enhance problem-solving abilities, build distress tolerance, increase motivation, and set and achieve goals.
- Modifying group counseling, so that groups are smaller and more structured than in traditional SUD treatment. Confrontational situations should be avoided. To be effective, each group session should focus on a particular skill or topic. For patients with unstable schizophrenia currently exhibiting uncontrolled positive symptoms, deferment of group counseling and continued individual counseling may be appropriate until stabilization occurs.

Learn more about treating patients with CODs in TIP 42 (<https://store.samhsa.gov/product/tip-42-substance-use-treatment-persons-co-occurring-disorders/PEP20-02-01-004>).

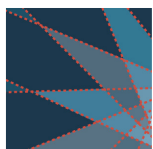


Summary

Patients who belong to specific populations with intrinsic vulnerabilities related to systems of care may have higher rates of stimulant use disorders and more difficulties engaging in care for these disorders. Factors that can influence treatment engagement among these special populations include location and availability of SUD programs and culturally competent clinicians, clinicians'

ability to foster trust and safe relationships, and clinicians' ability to apply individualized approaches. By understanding the needs of special populations with stimulant use disorders, as well as their care access issues and treatment considerations, clinicians can provide patient-centered, effective care that maximizes rapport and treatment engagement.

This page intentionally left blank.



Chapter 7—Resources

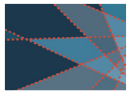
Resources for Counselors, Providers, and Programs

Substance Abuse and Mental Health Services Administration (SAMHSA), Addiction Technology Transfer Center (ATTC) Network (<https://attcnetwork.org>): The ATTC Network is a multidisciplinary resource for professionals in the substance use disorder (SUD) treatment and recovery services field. The network's 10 U.S.-based centers, 2 national focus area centers (the National American Indian & Alaska Native ATTC [<https://attcnetwork.org/centers/national-american-indian-and-alaska-native-attc/home>] and National Hispanic and Latino ATTC [<https://attcnetwork.org/centers/national-hispanic-and-latino-attc/home>]), and Network Coordinating Office provide news, tools and other resources, and free and low-cost training programs. The training includes a new series on contingency management (CM). Access the CM series at <https://attcnetwork.org/centers/northwest-attc/news/new-online-course-contingency-management-healthcare-settings> for Part 1 and <https://attcnetwork.org/centers/network-coordinating-office/contingency-management-part-2-founding-principles> for Part 2.

SAMHSA, Lesbian, Gay, Bisexual, and Transgender (LGBT) Behavioral Health Equity (<https://www.samhsa.gov/behavioral-health-equity/lgbt>): This webpage provides information on SAMHSA's programs related to the LGBT community and SAMHSA resources for providers and programs working with the LGBT population, as well as links to other federal initiatives that seek to expand services and improve behavioral health outcomes for these individuals.

SAMHSA, Mental Health Technology Transfer Center (MHTTC) Network (<https://mhttcnetwork.org>): The MHTTC Network supports resource development and dissemination, training and technical assistance, and workforce development for the mental health field. The network includes 10 Regional Centers, a National American Indian and Alaska Native Center (https://mhttcnetwork.org/sites/default/files/2020-12/AIAN_MHTTC_Year2_TwoPager%20edited.pdf), a National Hispanic and Latino Center (https://mhttcnetwork.org/sites/default/files/2020-12/NHL%20MHTTC%20Year%202_%202%20pager.pdf), and a Network Coordinating Office (<https://mhttcnetwork.org/centers/mhttc-network-coordinating-office/network-coordinating-office>). These centers work with healthcare systems, organizations, and treatment practitioners involved in the delivery of mental health services to strengthen their capacity to deliver effective evidence-based practices to individuals.

SAMHSA, Prevention Technology Transfer Center (PTTC) Network (<https://pttcnetwork.org>): The PTTC Network seeks to improve implementation and delivery of effective substance abuse prevention interventions and provides training and technical assistance services to the substance abuse prevention field. The network is comprised of 10 Domestic Regional Centers; 2 National Focus Area Centers, one focused on American Indians and Alaska Natives (<https://pttcnetwork.org/centers/national-american-indian-alaska-native-pttc/home>) and another focused on Hispanic and Latino populations (<https://pttcnetwork.org/centers/national-hispanic-latino-pttc/home>); and a Network Coordinating Office (<https://pttcnetwork.org/centers/pttc-network-coordinating-office/about-network-coordinating-office>). Together the network serves the 50 U.S. states, the District of Columbia, Puerto Rico, the U.S. Virgin Islands, and the Pacific Islands of Guam, American Samoa, Palau, the Marshall Islands, Micronesia, and the Mariana Islands.



SAMHSA, Providers Clinical Support System (PCSS) (<https://pcssnow.org>): The PCSS program was created in response to the opioid overdose epidemic to train primary care providers in the evidence-based prevention and treatment of opioid use disorder (OUD) and treatment of chronic pain. A coalition of major healthcare organizations, including the American Academy of Addiction Psychiatry, the American Medical Association, and the American Psychiatric Association (APA), the PCSS program provides a variety of trainings and clinical mentoring, with the goal of increasing healthcare providers' knowledge and skills in the prevention, identification, and treatment of SUDs, with a focus on OUD.

SAMHSA, Recovery Support Tools and Resources (<https://www.samhsa.gov/brss-tacs/recovery-support-tools-resources>): This webpage provides SAMHSA's working definition of recovery and links to information, tools, and video trainings relevant to shared decision-making, peer workers, and programs led by parents, families, and youth and young adults.

SAMHSA/National Center on Substance Abuse and Child Welfare, Research on Methamphetamine (<https://ncsacw.samhsa.gov/resources/methamphetamine/literature-review.aspx>): This webpage provides citations for peer-reviewed research on topical areas related to methamphetamine (MA), including prenatal exposure; children and family affected by MA use; prevalence, intervention, and treatment; criminal justice and legislation; and special populations and how they have been impacted by MA.

APA Presidential Task Force to Address Structural Racism Throughout Psychiatry (<https://www.psychiatry.org/psychiatrists/structural-racism-task-force>): This resource provides psychiatric clinicians with information about structural racism and mental health services. It includes continuing medical education programs for psychiatrists, recommended reading, and video recordings of town hall gatherings that address structural racism.

Association of Lesbian, Gay, Bisexual, Transgender Addiction Professionals and Their Allies (NALGAP) (www.nalgap.org): NALGAP's mission is to confront oppression and discriminatory practices in the delivery of services to all people and to advocate for programs and services that affirm all genders and sexual orientations. NALGAP provides information, training, networking, and advocacy about addiction and related issues, and support for health professions and individuals in recovery.

Colorado Meth Project, Resources (<https://coloradomethproject.org/resources/#:~:text=Ask%20MethProject.org%20is%20an%20integrated%20campaign%20to%20reduce,radio%2C%20print%2C%20online%2C%20mobile%2C%20and%20social%20media%20campaigns>): The Colorado Meth Project seeks to reduce the use of MA through public service messaging, community outreach, and public policy. A key component of the program is MethProject.org, which features TV, radio, print, online, mobile, and social media campaigns that communicate the risks of MA use.

Generation Rx, Educational Toolkits for Safe Medication Practices (<https://generationrx.org/toolkits/>): The mission of Generation Rx is to educate people of all ages about the dangers of prescription medication misuse. Developed through a partnership between The Ohio State University College of Pharmacy and the Cardinal Health Foundation, the Generation Rx website provides open-source, ready-to-use resources designed to help educators and providers make presentations or develop prevention programs in communities or academic environments.

Methamphetamine Research Center (MARC) (<https://www.ohsu.edu/methamphetamine-research-center>): Part of the Oregon Health & Science University, MARC is funded by the National Institute on Drug Abuse (NIDA) to study genetic factors in human and animal responses to MA, with the goal of identifying new approaches to treatment.

Motivational Interviewing Network of Trainers (MINT) (<https://motivationalinterviewing.org>):

MINT works to establish and promote good practice in the use, research, and training of motivational interviewing (MI). The MINT website provides users with a library of MI publications, as well as references, articles, videos, and links to training opportunities in the theory and practice of MI.

NAADAC, The Association for Addiction Professionals (<https://www.naadac.org/resources>):

NAADAC provides free training and low-cost continuing education credits for SUD professionals. Topics covered include SUD treatment, supervision, workforce development, veterans, families, trauma, and peer recovery support.

National Institute on Alcohol Abuse and Alcoholism (NIAAA), Professional Education Materials (<https://www.niaaa.nih.gov/alcohol-effects-health/professional-education-materials>):

This NIAAA webpage is for clinicians, physicians, social workers, and other providers who work with people who misuse alcohol. It offers access to screening, brief intervention, treatment planning, and general information.

NIDA, Division of Therapeutics and Medical Consequences (<https://www.drugabuse.gov/about-nida/organization/divisions/division-therapeutics-medical-consequences-dtmc/research-programs>): This resource supports and conducts studies to evaluate the safety and efficacy of pharmacotherapies, behavioral therapies, and devices to treat SUDs.**NIDA, Motivational Incentives Package** (<https://www.drugabuse.gov/nidamed-medical-health-professionals/ctn-dissemination-initiative/motivational-incentives-package-proven-approach-to-treatment>): This NIDA webpage provides behavioral healthcare practitioners with access to motivational incentive tools for engaging clients in behavioral health therapy.

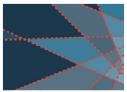
NIDAMED, Clinical Resources (<https://www.drugabuse.gov/nidamed-medical-health-professionals>): The NIDAMED website provides healthcare professionals with science-based information about the effects of substance misuse on clients' health, such as how to identify substance use early and prevent it from turning into misuse or addiction.

NIDA, Quick Screen V1.0 (<https://www.drugabuse.gov/sites/default/files/pdf/nmassist.pdf>): Clinicians can use this tool to screen patients age 18 or older for general substance misuse. This resource also includes questions from the NIDA-Modified Alcohol, Smoking, and Substance Involvement Screening Test V2.0 that inquire about recent and lifetime use of specific substances.

NIDA/SAMHSA, Motivational Incentives Suite (<https://collaborativeforhealth.org/bettertxoutcomes/>): The Motivational Incentives Suite is a collection of tools and resources to help organizations understand and implement CM into practice.

Self-Management Resource Center (<https://www.selfmanagementresource.com/>): The center's website offers a range of small-group, self-management programs for chronic illness. Programs are available online or through licensed local organizations. In addition to the core program for groups with multiple chronic illnesses, several condition-focused programs are offered, including diabetes, chronic pain, and HIV.

Trauma Informed Oregon, Trauma Informed Urine Drug Screenings (<https://traumainformedoregon.org/wp-content/uploads/2019/05/Urine-Drug-Screen-tip-sheet.pdf>): Urine drug screens (UDS) can be triggering experiences for some people, especially those with a history of trauma. This tip sheet can be used to inform the UDS procedure, with the goals of preventing re-traumatization of patients and facilitating their safety. Included are guiding considerations, tips, and examples offered by service users and experts in the substance use treatment field.



U.S. Department of Veterans Affairs (VA), National Center for PTSD (<https://www.ptsd.va.gov/professional/index.asp>): VA offers training materials, information, and tools to assess and treat trauma-related disorders. This website contains links to continuing education on posttraumatic stress disorder (PTSD), free training in prolonged exposure therapy for providers who treat veterans, and links to VA benefits.

Publications

SAMHSA Publications

After Incarceration: A Guide to Helping Women Reenter the Community (<https://store.samhsa.gov/product/After-Incarceration-A-Guide-To-Helping-Women-Reenter-the-Community/PEP20-05-01-001>): This guide provides an overview of topics and resources for supporting women who are reentering the community after involvement with the criminal justice system. It was created for individuals who provide or coordinate reentry services (e.g., corrections staff, reentry organizations, substance use disorder and mental health treatment providers, reentry specialists, peer specialists).

Advisory: Hepatitis C Screening in the Behavioral Healthcare Setting (<https://store.samhsa.gov/product/Advisory-Hepatitis-C-Screening-in-the-Behavioral-Healthcare-Setting/sma15-4917>): Part of SAMHSA's Advisory series, this brief guide gives an overview of hepatitis C and discusses approaches to testing, treatment, and counseling.

Advisory: Integrating Vocational Services Into Substance Use Disorder Treatment (https://store.samhsa.gov/product/integrating-vocational-services-substance-use-disorder-treatment/pep20-02-01-019?referer=from_search_result): This Advisory is directed to programs serving clients who are unemployed, underemployed, or struggling in workplace settings. It presents strategies and resources for SUD treatment counselors and clinic directors to improve outcomes for clients in recovery by helping them find and keep employment and manage workplace stressors.

Anger Management for Substance Use Disorder and Mental Health Clients: A Cognitive—Behavioral Therapy Manual (<https://store.samhsa.gov/product/PEP19-02-01-001>): This treatment manual describes the concept of cognitive—behavioral therapy (CBT) and its use of social learning theory for treating clients in a variety of clinical settings. CBT teaches clients with substance use and mental disorders how to control their anger and disrupt the aggression cycle. The manual may be used with the companion *Participant Workbook* (see entry below).

Anger Management for Substance Use Disorder and Mental Health Clients: Participant Workbook (<https://store.samhsa.gov/product/PEP19-02-01-002>): This workbook was developed for use with *Anger Management for Substance Use Disorder and Mental Health Clients: A Cognitive—Behavioral Therapy Manual*. Participants refer to the workbook during anger management group treatment and use it to complete homework assignments.

Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants (<https://store.samhsa.gov/product/Clinical-Guidance-for-Treating-Pregnant-and-Parenting-Women-With-Opioid-Use-Disorder-and-Their-Infants/SMA18-5054>): This guide recommends standard and feasible approaches to the care of pregnant and parenting women with OUD and their infants. These approaches can be adopted in a variety of care settings.

Finding Quality Treatment for Substance Use Disorders (<https://store.samhsa.gov/product/PEP18-TREATMENT-LOC>): This resource is for people seeking behavioral health services and treatment for SUDs. It provides guidance on how to find a quality treatment center and the steps to complete before accessing treatment.

Guidance Document for Supporting Women in Co-ed Settings (www.samhsa.gov/resource/ebp/guidance-document-supporting-women-co-ed-settings): Most women in SUD treatment receive services in co-ed treatment and recovery centers where men outnumber women, yet women and men with SUDs differ in many ways. This guide explores the ways in which treatment providers can better understand these differences and meet women's specific treatment needs.

In Brief: Rural Behavioral Health: Telehealth Challenges and Opportunities (<https://store.samhsa.gov/product/SMA16-4989>): This guide for behavioral healthcare providers describes the barriers associated with implementing telehealth services in rural and frontier communities and offers tips on how to overcome these challenges and improve patient outcomes.

In Brief: Treating Sleep Problems of People in Recovery From Substance Use Disorders (<https://store.samhsa.gov/product/SMA14-4859>): This publication explains how healthcare providers can help clients in recovery from SUDs who have sleep problems. It discusses the potential impact of poor sleep on recovery and offers recommendations on screening and treatment.

Matrix Intensive Outpatient Treatment for People With Stimulant Use Disorders: Client's Handbook (<https://store.samhsa.gov/product/SMA15-4154>): This handbook contains checklists and other recovery tools based on the Matrix model, including tips for managing emotions, substance use triggers, and other impediments to achieving and maintaining recovery from stimulant misuse.

Matrix Intensive Outpatient Treatment for People With Stimulant Use Disorders: Counselor's Treatment Manual (<https://store.samhsa.gov/product/SMA13-4152>): This manual is one of five components of the Matrix model's intensive outpatient treatment package that provides structured, evidence-based treatment strategies for helping clients who misuse or are dependent on stimulant drugs, such as MA and cocaine.

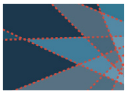
Preventing the Use of Marijuana: Focus on Women and Pregnancy (<https://www.samhsa.gov/resource/ebp/preventing-use-marijuana-focus-women-pregnancy>): This guide examines the scientific literature on the risk factors for, and the adverse health consequences of, marijuana use during pregnancy. It also discusses emerging and best practices to prevent or reduce this use.

Prevention and Treatment of HIV Among People Living with Substance Use and/or Mental Disorders (<https://store.samhsa.gov/product/Prevention-and-Treatment-of-HIV-Among-People-Living-with-Substance-Use-and-or-Mental-Disorders/PEP20-06-03-001>): This guide provides an overview of interventions for people living with substance use and/or mental health issues who are at risk for, or are living with, HIV. The interventions addressed are in alignment with the goals of the federal "Ending the HIV Epidemic: A Plan for America" initiative.

Principles of Community-based Behavioral Health Services for Justice-involved Individuals: A Research-based Guide (<https://store.samhsa.gov/product/Principles-of-Community-based-Behavioral-Health-Services-for-Justice-involved-Individuals-A-Research-based-Guide/SMA19-5097>): This guide, intended for behavioral health service providers in community settings, shares foundational principles for sound clinical practice and community-based case management when helping criminal justice-involved individuals with mental disorders and SUDs.

A Provider's Introduction to Substance Abuse Treatment for Lesbian, Gay, Bisexual, and Transgender Individuals (<https://store.samhsa.gov/product/Providers-Introduction-Substance-Abuse-Treatment-Lesbian-Gay-Bisexual-Transgender/SMA12-4104>): This manual assists behavioral health clinicians in providing services that are sensitive to transgender and other clients from LGBT communities.

Recovery-Oriented Systems of Care (ROSC) Resource Guide (www.samhsa.gov/sites/default/files/rosc_resource_guide_book.pdf): This resource guide explains what a ROSC is and the planning and implementation steps necessary to establish one. The guide also includes links to studies, white papers, presentations, manuals, practice guides, checklists, regulations, and other resources that can help with the formation of a ROSC.



SAMHSA and the National Association of State Alcohol and Drug Abuse Directors, Addressing the Substance Use Disorder (SUD) Service Needs of Returning Veterans and Their Families (<https://www.samhsa.gov/sites/default/files/veterans-report.pdf>): This resource addresses the training needs of state alcohol and drug agencies and treatment providers responsible for administering behavioral health services to returning veterans and their families. It includes a collection of case studies, a discussion guide, and a list of provider resources organized by state.

SAMHSA's Concept of Trauma and Guidance for a Trauma-Informed Approach (<https://store.samhsa.gov/product/SMA14-4884>): This manual provides a working concept of trauma and key principles of a trauma-informed treatment approach that can be used by behavioral health workers and an array of service systems. It also suggests methods for implementing a trauma-informed approach.

Take Action Against Hepatitis C (<https://store.samhsa.gov/product/Take-Action-Against-Hepatitis-C/sma14-4853>): Using a comic book format and plain language, this publication covers basic information about what hepatitis is, how to reduce infection risk, and screening and treatment processes and options.

Tips for Teens: The Truth About Cocaine (<https://store.samhsa.gov/product/PEP18-01>): This resource is a concise presentation of cocaine's harmful effects on the brain and body. It features a question-and-answer section on trend data and risks, the outward signs of cocaine use, and information on how to access treatment from SAMHSA.

Treatment of Stimulant Use Disorders (<https://store.samhsa.gov/product/PEP20-06-01-001>): This guide discusses effective practices to treat SUDs, clinical challenges associated with these disorders, and implementation strategies to address those challenges.

SAMHSA Treatment Improvement Protocols (TIPs)

TIP 26: Treating Substance Use Disorders in Older Adults (<https://store.samhsa.gov/product/treatment-improvement-protocol-tip-26-treating-substance-use-disorder-in-older-adults/PEP20-02-01-011>): TIP 26 helps providers and others better understand how to identify, manage, and prevent substance misuse in older adults. It describes the unique ways in which the signs and symptoms of SUD manifest in older adults; drug and alcohol use disorder screening tools, assessments, and treatments specifically tailored for older clients' needs; the interaction between SUDs and cognitive impairment; and strategies to help providers improve their older clients' social functioning and overall wellness.

TIP 27: Comprehensive Case Management for Substance Abuse Treatment (<https://store.samhsa.gov/product/SMA15-4215>): TIP 27 describes case management as an interdisciplinary approach to SUD treatment that includes coordination of health care, substance use, mental health, and social services. It provides guidance and resources to keep clients engaged in treatment and moving toward recovery.

TIP 31: Screening and Assessing Adolescents for Substance Use Disorders (<https://store.samhsa.gov/product/SMA12-4079>): TIP 31 describes strategies, procedures, and screening and assessment instruments that are appropriate for the initial detection of substance use among adolescents, the comprehensive assessment of their problems, and subsequent treatment planning. It summarizes each instrument in the appendixes.

TIP 34: Brief Interventions and Brief Therapies for Substance Abuse (<https://store.samhsa.gov/product/SMA12-3952>): TIP 34 documents the components of and criteria for using CBT, brief strategic and interactional therapies, brief humanistic and existential therapies, brief psychodynamic therapy, short-term family therapy, and time-limited group therapy.

TIP 35: *Enhancing Motivation for Change in Substance Use Disorder Treatment* (<https://store.samhsa.gov/product/PEP19-02-01-003>): TIP 35 describes the elements of motivational interventions, the five principles of MI, catalysts for changing behavior, and the stages of change that clients go through while working toward recovery from SUDs.

TIP 38: *Integrating Substance Abuse Treatment and Vocational Services* (<https://store.samhsa.gov/product/TIP-38-Integrating-Substance-Abuse-Treatment-Vocational-Services/SMA12-4216>): TIP 38 offers practice guidelines and recommendations for integrating employment services into SUD treatment. It also provides information about funding, policy, and legal issues.

TIP 39: *Substance Use Disorder Treatment and Family Therapy* (<https://store.samhsa.gov/product/treatment-improvement-protocol-tip-39-substance-use-disorder-treatment-and-family-therapy/PEP20-02-02-012>): TIP 39 helps providers and administrators better understand how to include families in SUD treatment and services.

TIP 42: *Substance Use Disorder Treatment for People With Co-Occurring Disorders* (<https://store.samhsa.gov/product/PEP20-02-01-004>): TIP 42 provides guiding principles and strategies for working with people who have co-occurring mental disorders and SUDs.

TIP 44: *Substance Abuse Treatment for Adults in the Criminal Justice System* (<https://store.samhsa.gov/product/SMA13-4056>): TIP 44 addresses both clinical and programmatic areas of treatment for men and women involved in the criminal justice system. It guides counselors and administrators on best practices for intervening throughout the justice process. The 2017 Editor's Note features legislative, literature, and clinical updates.

TIP 51: *Substance Abuse Treatment: Addressing the Specific Needs of Women* (<https://store.samhsa.gov/product/SMA15-4426>): TIP 51 considers the complex and unique facets of women's social, socioeconomic, cultural, and health needs that should be considered when providing treatment services for SUD.

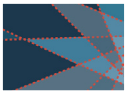
TIP 55: *Behavioral Health Services for People Who Are Homeless* (<https://store.samhsa.gov/product/SMA15-4734>): TIP 55 focuses on proven approaches for providing screening/assessment, treatment planning, and continuing care to clients who are homeless or at risk of being homeless. Vignettes based on role-played interactions feature techniques that can be applied in a variety of settings.

TIP 57: *Trauma-Informed Care in Behavioral Health Services* (<https://store.samhsa.gov/product/SMA14-4816>): TIP 57 covers trauma awareness, the impact of trauma, trauma-informed screening and assessment, implementation of trauma-informed care, and development of a trauma-informed workforce.

TIP 59: *Improving Cultural Competence* (<https://store.samhsa.gov/product/SMA15-4849>): TIP 59 provides an introduction to cultural competence in behavioral health services. The TIP is written for treatment counselors, clinical and programmatic staff, and program administrators and discusses racial, ethnic, and cultural considerations.

TIP 60: *Using Technology-Based Therapeutic Tools in Behavioral Health Services* (<https://store.samhsa.gov/product/SMA15-4924>): TIP 60 introduces behavioral health service providers to technology-based treatment and prevention tools and interventions that can be used in various behavioral health service settings. The TIP includes guidelines for implementation, as well as ethical, programmatic, and regulatory considerations for counselors and administrators.

TIP 61: *Behavioral Health Services for American Indians and Alaska Natives* (<https://store.samhsa.gov/product/TIP-61-Behavioral-Health-Services-For-American-Indians-and-Alaska-Natives/SMA18-5070>): TIP 61 provides guidance to behavioral health program clinicians and administrators about the importance of cultural awareness, cultural competence, and culture-specific knowledge when working with American Indian and Alaska Native clients.



TIP 63: Medications for Opioid Use Disorder (<https://store.samhsa.gov/product/PEP20-02-01-006>): TIP 63 introduces the three U.S. Food and Drug Administration (FDA)-approved medications for OUD treatment and explains their use in general medical settings. It includes practical guidelines and clinical tools for OUD screening, assessment, diagnosis, treatment planning, and referral to recovery support services.

Other Agency Publications

American Academy of Pediatrics, Substance Use Screening, Brief Intervention, and Referral to Treatment (<https://pediatrics.aappublications.org/content/138/1/e20161211>): This resource provides policy and clinical guidance to help pediatricians incorporate screening, brief intervention, and referral to treatment for substance misuse among adolescent patients.

American Addiction Centers, How to Help a Meth Addict (<https://drugabuse.com/methamphetamine/how-to-help-an-addict/>) and **Meth Addiction, Abuse, and Treatment** (<https://americanaddictioncenters.org/meth-treatment>): These guides offer an overview of the nature and signs of MA misuse, discuss effective ways to approach a loved one who may be misusing MA, discuss the types of treatment available, and provide resources for individuals and families who are seeking help for SUD.

Boston Public Health Commission's Needle Exchange Program, Access Harm Reduction Overdose Prevention and Education (AHOPE), Program Participant Guide (<https://www.bphc.org/whatwedo/Recovery-Services/services-for-active-users/Documents/Client%20Manual%20FINAL.pdf>): The AHOPE Needle Exchange Program was created to reduce the spread of infectious diseases like HIV/AIDS, hepatitis C, and tuberculosis among individuals who inject illicit drugs, as well as their sexual and drug use partners. The guide focuses on "safer" drug use and injection practices and provides information about the health risks of injecting illicit drugs, overdose prevention, and services available to people who use illicit drugs.

Centers for Disease Control and Prevention (CDC), Viral Hepatitis Webpage (<https://www.cdc.gov/hepatitis/index.htm>): This webpage provides a broad range of information on viral hepatitis, including a definition of all strains (A through E), hepatitis trends in the United States, national and global prevalence statistics, and resources for treatment and prevention.

Government of South Australia, SA Health, Acute Presentations Related to Methamphetamine Use: Clinical Guideline for Adults (https://www.sahealth.sa.gov.au/wps/wcm/connect/b1f536a1-eb41-469c-997c-ed5a67fd4a29/+Guideline+Management+acute+methamphetamine_v2.0_03.06.2019.pdf?MOD=AJPERES∓CACHEID=ROOTWORKSPACE-b1f536a1-eb41-469c-997c-ed5a67fd4a29-nqXZ1er): This statewide guideline aims to promote best practice management of adult patients who present to urgent care in an agitated state. It promotes the use of a standardized assessment for the possible use of MA or related substances, while using the AGRO+ approach for safely and respectfully de-escalating the agitated behavior of the patient.

National Harm Reduction Coalition, Getting Off Right: A Safety Manual for Injection Drug Users (<https://harmreduction.org/issues/safer-drug-use/injection-safety-manual/>): This step-by-step guide to safer drug injection focuses on how to avoid disease, reduce accident and injury, and recognize and respond to overdose. It also covers the potential health complications of injecting drugs.

Minnesota Department of Health, Opioids: Social Determinants of Substance Use & Overdose Prevention (<https://www.health.state.mn.us/communities/opioids/prevention/socialdeterminants.html>): This webpage provides an overview of social determinants of health, and discusses the ways in which individual, interpersonal, community, and societal determinants can influence an individual's use or misuse of substances.

NAADAC, the Association for Addiction Professionals: Counseling African Americans With Substance Use Disorders (https://www.naadac.org/assets/2416/2015-06-04_counseling_african_americans_with_suds_webinarslides.pdf):

This PowerPoint presentation showcases tools that can help practitioners work more effectively with African American clients who are dealing with chemical dependency and other SUDs.

National Center on Substance Abuse and Child Welfare, Children Affected by Methamphetamine Program: Implementation Progress and Performance Measurement Report (<https://ncsacw.samhsa.gov/topics/methamphetamine.aspx>): This page offers resources and guidelines for meeting the needs of parents and children affected by MA use, including this summary report for a grant program focused on providing services to children ages 0–17 and their families.

NIDA, Methamphetamine Resource Report (<https://www.drugabuse.gov/download/37620/methamphetamine-research-report.pdf?v=f6a96a8721a56a0f765889a3d3e678c7>): Revised in October 2019, this report provides an overview of the latest scientific findings on MA, including short- and long-term health consequences, effects on pregnancy, and prevention and treatment options.

NIDA, Mind Matters: The Body's Response to Prescription Stimulants (<https://teens.drugabuse.gov/teachers/lessonplans/mind-matters-bodys-response-prescription-stimulants>): This colorful booklet is designed for educators of fifth- through ninth-graders, to help teach students about the uses of prescription stimulants and the dangers of misusing these drugs.

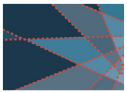
NIDA, Prescription Stimulant Medications (Amphetamines) (<https://teens.drugabuse.gov/drug-facts/prescription-stimulant-medications-amphetamines>): This publication provides an overview of prescription stimulants, how misuse of these drugs can occur, the risks of overdose, and how to find treatment for misuse, as well as links to resources for educators.

NIDA, Prescription Stimulants DrugFacts (<https://www.drugabuse.gov/publications/drugfacts/prescription-stimulants>): This publication provides an overview of prescription stimulants, how they can be misused, the risks of overdose, and how to get treatment for misuse of these drugs.

NIDA, Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition), Community Reinforcement Approach Plus Vouchers (Alcohol, Cocaine, Opioids) (<https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral-therapies/community-reinforcement-approach-vouchers>): This resource describes the Community Reinforcement Approach (CRA) Plus Vouchers, an intensive 24-week outpatient therapy that combines counseling, vocational services, recreational and social activities, and material incentives to help patients maintain abstinence.

NIDA, Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition), Contingency Management Interventions/Motivational Incentives (Alcohol, Stimulants, Opioids, Marijuana, Nicotine) (<https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral-therapies/contingency-management-interventions-motivational-incentives>): This resource briefly summarizes how to implement two approaches to CM, Voucher-Based Reinforcement and Prize Incentives CM.

Oregon Post Adoption Resource Center, Parenting Children Who Have Been Exposed to Methamphetamine: A Brief Guide for Adoptive, Guardianship, and Foster Parents (<https://www.ohsu.edu/sites/default/files/2019-06/Parenting-Children-Who-Have-Been-Exposed-to-Methamphetamine.pdf>): This guide provides an overview of MA and its pre- and postnatal effects on children. It also offers guidance to parents who are caring for children who were exposed to MA.



Rural Health Information Hub, *Substance Use and Misuse in Rural Areas* Webpage (<https://www.ruralhealthinfo.org/topics/substance-use>):

This webpage answers frequently asked questions regarding substance use and misuse in rural areas, addresses prevalence and usage trends in these areas, and provides links to prevention and treatment resources.

UCLA, Integrated Substance Abuse Programs, *A Treatment Manual for Implementing Contingency Management* (http://www.uclaisap.org/assets/documents/Manual%20for%20Implementing%20Contingency%20Management_11-8-2011%20clean.pdf): This online treatment manual describes how to implement a CM program for individuals who were recently paroled and are seeking SUD treatment in the community.

United Nations Office on Drugs and Crime, *Treatment of Stimulant Use Disorders: Current Practices and Promising Perspectives* (https://www.unodc.org/documents/drug-prevention-and-treatment/Treatment_of_PSUD_for_website_24.05.19.pdf): This discussion paper describes the physical and behavioral consequences of using stimulants for both medical and illicit purposes, explains stimulant use disorder, and provides information on evidence-based treatment interventions.

U.S. Department of Health and Human Services, *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health* (<https://addiction.surgeongeneral.gov/sites/default/files/surgeon-generals-report.pdf>):

This report alerts the American public about the burden of substance misuse in communities, the effects of government policies on prevention and treatment, and opportunities for increasing access to treatment for all those affected by SUDs.

U.S. Department of Housing and Urban Development (HUD), *Housing First in Permanent Supportive Housing Brief* (<https://www.hudexchange.info/resource/3892/housing-first-in-permanent-supportive-housing-brief/>): This brief for supportive housing providers is a high-level summary of the Housing First approach and offers some initial steps for providers interested in adopting it.

U.S. Department of Justice/Drug Enforcement Administration, *Drug Fact Sheet—Methamphetamine* (https://www.dea.gov/sites/default/files/2020-06/Methamphetamine-2020_0.pdf):

This fact sheet provides an overview of MA, including its origin, common names, effects on the brain and body, and the risks of misuse and overdose.

HUD, *The 2019 Annual Homeless Assessment Report (AHAR) to Congress* (<https://www.huduser.gov/portal/sites/default/files/pdf/2019-AHAR-Part-1.pdf>): This report outlines key findings of the 2019 Point-In-Time count and Housing Inventory count, which provides national, state, and local estimates of overall homelessness and subgroup-specific data.

World Health Organization, *International Classification of Diseases, Clinical Modification (ICD–CM)* (under “Coding” at <https://www.cms.gov/Medicare/Medicare>): Providers can use criteria from this publication to confirm patient diagnoses and to determine treatment codes for proper reimbursement. (The current version at the time of this TIP update’s publication was ICD-10-CM.)

Yale University Psychotherapy Development Center, *Contingency Management: Using Motivational Incentives to Improve Drug Abuse Treatment* (<http://lib.adai.washington.edu/ctnlib/PDF/CMmanual.pdf>): Research on the use of CM interventions shows the efficacy of providing tangible incentives to clients who are targeting distinct behaviors on their journey to achieving recovery from SUDs. This publication provides an overview of research findings and guides practitioners on applying CM strategies across clinical settings.

Treatment Locators

SAMHSA's Behavioral Health Treatment Services Locator (<https://findtreatment.samhsa.gov/>): This confidential and anonymous information source is for people seeking facilities for treating mental disorders and/or SUDs in the United States or U.S. territories. It also offers information about treatment options and how to pay for treatment.

SAMHSA's National Directory of Drug and Alcohol Abuse Treatment Facilities, 2019 (<https://www.samhsa.gov/data/report/national-directory-drug-and-alcohol-abuse-treatment-facilities-2019>):

This directory provides a comprehensive list of state-certified substance use and mental disorder treatment facilities that responded to the 2018 National Survey of Substance Abuse Treatment Services. It lists SUD agencies and individual treatment facilities by city and state.

NIAAA Alcohol Treatment Navigator (<https://alcoholtreatment.niaaa.nih.gov/>): This resource provides information about treatment for alcohol misuse and how to choose a high-quality treatment provider, center, or program for alcohol use disorder.

VA SUD Program Locator (<https://www.va.gov/directory/guide/SUD.asp>): This webpage lets users search by state for VA medical centers that offer specialized SUD treatment.

Client and Family Resources

Organizations

SAMHSA's National Helpline (<https://www.samhsa.gov/find-help/national-helpline>; 1-800-662-HELP [4357]; 1-800-487-4889 [TTY]): This helpline provides free treatment referral and relevant information for individuals who need help dealing with substance misuse or mental illness. Phone lines are staffed 24 hours a day by information specialists who can respond in English or Spanish. All calls to the helpline are free and confidential.

Anxiety & Depression Association of America (ADAA) (<https://adaa.org>): ADAA promotes awareness of anxiety disorders and depression and supports scientific innovation in treatment. The website contains information and links to education, treatment, resources, and support for consumers, the public, and treatment providers.

Association of Recovery Community Organizations (ARCO) (<https://facesandvoicesofrecovery.org/arco/>): ARCO supports a growing network of local, regional, and statewide recovery community organizations (RCOs). It links RCOs with local and national allies and provides training and technical assistance to recovery groups.

Attention Deficit Disorder Association (ADDA) (<https://add.org>): ADDA is an international nonprofit organization founded to help adults with attention deficit/hyperactivity disorder (ADHD) lead better lives. ADDA brings together scientific perspectives and lived experiences to generate hope, awareness, empowerment, and connections in the field of ADHD.

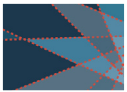
Defense Health Agency (DHA) (<https://www.health.mil/About-MHS/OASDHA/Defense-Health-Agency>): DHA is a joint, integrated combat support agency and the healthcare delivery arm of the Military Health System (<https://www.health.mil>). It supports the delivery of integrated, affordable, and high-quality health services and manages a global healthcare network of military hospitals and clinics.

Learn to Cope (<https://www.learn2cope.org/>): This secular mutual-support group offers education, resources, and peer support for families of people with SUDs, focusing on OUD. It maintains an online forum and convenes groups in several states.

Legal Action Center (LAC) (<https://www.lac.org>): LAC offers information about the rights of people with criminal records, HIV/AIDS, and SUDs.

Mental Health America (<https://www.mhanational.org/>): This nonprofit, community-based organization aims to improve public knowledge of mental disorders and enhance prevention and treatment strategies. It is composed of more than 200 affiliates in 41 states, 6,500 affiliate staff members, and more than 10,000 volunteers.

National Alliance on Mental Illness (NAMI) (<https://www.nami.org/Home>): NAMI is the largest grassroots educational, peer support, and mental health advocacy organization in the United States. Founded in 1979 by a group of family members of people with mental disorders, it has grown to become an association of hundreds of local affiliates, state organizations, and volunteers.



National Coalition Against Prescription Drug Abuse (NCAPDA) (www.ncapda.org): NCAPDA is a nonprofit, volunteer-based organization established to prevent prescription SUD and overdose deaths through community education and policy change at the local, state, and national levels. Its goal is to network with similar organizations and like-minded agencies throughout the country to share best practices, develop and share useful material resources, and establish and implement a cohesive, nationwide education campaign around medication safety.

National Council on Alcoholism and Drug Dependence of the Central Mississippi Area (NCADD) (<http://ncaddms.org>): NCADD offers a variety of publications and resources and has a nationwide network of nearly 100 affiliates. These affiliates provide information and referrals to local services, including counseling and treatment.

National Empowerment Center (<http://power2u.org>): The center has an extensive resource list that includes a directory of consumer-run organizations, peer support, and webinars.

National Suicide Prevention Lifeline (<http://suicidepreventionlifeline.org>; 1-800-273-8255): Funded by SAMHSA, this national network of local crisis centers offers free and confidential support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week.

Parents of Addicted Loved Ones (PAL) (<http://palgroup.org>): This organization provides secular support group meetings for parents who have a child with an SUD. PAL hosts in-person meetings in some locations, as well as online and phone meetings.

Mutual-Help Programs

Al-Anon Family Groups (<http://al-anon.org>): Al-Anon meetings allow friends and family members of people who misuse substances to share their experiences and learn how to apply the principles of the Al-Anon program to their individual situations.

Alcoholics Anonymous® (AA) (<http://www.aa.org>): The AA website offers information about alcohol misuse and links to local resources that list AA meetings for people who misuse alcohol and want to stop. AA sponsors provide personal support from individuals with lived experience following 12-Step principles.

Cocaine Anonymous® (CA) World Services, Inc. (<http://ca.org>): CA is a mutual-help program for people with cocaine use disorder. It follows the 12-Step principles and offers meetings worldwide.

Crystal Meth Anonymous® (CM-Anon) (<http://www.crystalmeth.org>): CM-Anon is a fellowship program for people who use crystal meth and is based on the 12-Step principles. It includes a 24-hour helpline and has a directory of online and in-person meetings worldwide.

Emotions Anonymous (EA) (<http://emotionsanonymous.org>): EA is a 12-Step fellowship based on AA principles for people with emotional difficulties (not only clinical mental disorders). Groups are located in more than 30 countries and are available through Skype and phone meetings.

Faces & Voices of Recovery, Mutual Aid Resources (<http://facesandvoicesofrecovery.org/resources/mutual-aid-resources/>): Faces & Voices of Recovery offers information on mutual-help organizations in the following categories: 12-Step groups; alcohol use; co-occurring health conditions; faith-based organizations; family-, friend-, and youth-focused groups; gender-specific meetings; medication-assisted treatment; and secular groups.

Nar-Anon Family Groups (<http://www.nar-anon.org>): Nar-Anon group meetings are for friends and family members of people misusing narcotics and other substances. Group members share their experiences and learn to apply the 12-Step principles to their lives. Nar-Anon offers individualized support from experienced members acting as sponsors.

Narcotics Anonymous (NA) World Services (<https://www.na.org/>): NA is a global, community-based organization with a multilingual, multicultural membership that supports SUD recovery via a 12-Step program, including regular group meetings. This ongoing support network helps participants maintain a drug-free lifestyle.

National Mental Health Consumers' Self-Help Clearinghouse (<https://www.mhselfhelp.org/>): This clearinghouse offers a resource kit featuring the names and contact information of treatment and mutual-help support services that address SUDs and cooccurring disorders.

Partnership to End Addiction (<https://drugfree.org/>): Partnership to End Addiction is an online resource for families of individuals who use drugs, including stimulants. In addition to educational resources, the website includes a helpline, an online support community, peer-to-peer parent coaching, online skill-building courses, and a text message program that provides customized messages and resources. Resources are available in Spanish.

Pills Anonymous World Service (<https://www.pillsanonymous.org/>): This 12-Step mutual-help fellowship holds regular meetings for individuals in recovery from SUDs involving medication. Meeting participants share their experiences, build their strengths, and offer hope for recovery to one another.

Recoveries Anonymous (<https://www.r-a.org/>): This 12-Step mutual-help fellowship welcomes people with a broad range of problems, from SUDs to mental disorders to “problem behaviors” (e.g., compulsive spending, risk-taking, suicidal behaviors).

Secular Organizations for Sobriety (SOS) (<http://www.sossobriety.org/>): SOS is a nonprofit network of autonomous, nonprofessional local groups whose focus is on using a secular approach to maintaining abstinence from alcohol, other drugs, or other types of addictive behaviors.

SMART Recovery® (<https://www.smartrecovery.org/>): The SMART Recovery website provides information about the organization's science-based and self-empowering program, training opportunities, and a searchable database of local and online meetings in the United States and abroad.

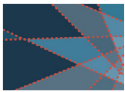
The Trevor Project (<https://www.thetrevorproject.org/>): The Trevor Project provides crisis intervention and suicide prevention services to lesbian, gay, bisexual, transgender, and queer & questioning (LGBTQ) young people age 24 and younger. The organization offers no-cost, judgment-free, online, hotline, and chat/text services that are available 24/7 to young people who want to socially network, are in crisis, or have questions about sexual orientation, gender identity, and other topics.

Women for Sobriety (WFS) (<https://womenforsobriety.org/>): WFS is a recovery program based on women's unique emotional needs. It focuses on helping women with SUDs begin and maintain recovery. WFS has certified moderators and chat leaders who facilitate mutual-help groups online and in person, as well as phone volunteers available for one-on-one support.

Laws and Regulations

SAMHSA, Fact Sheet: SAMHSA 42 CFR Part 2 Revised Rule (<https://www.hhs.gov/about/news/2020/07/13/fact-sheet-samhsa-42-cfr-part-2-revised-rule.html>): This resource provides a summary of changes to 42 CFR Part 2 (made in response to the opioid epidemic) pertaining to patient records in federally assisted SUD treatment programs.

SAMHSA, Substance Abuse Confidentiality Regulations (<https://www.samhsa.gov/about-us/who-we-are/laws-regulations/confidentiality-regulations-faqs>): This webpage provides information about consent and confidentiality regulations pertaining to release of patient records for SUD, as codified in 42 CFR Part 2 (revised).



CDC, Public Health Professionals Gateway, Health Insurance Portability and Accountability Act of 1996 (HIPAA) (<https://www.cdc.gov/phlp/publications/topic/hipaa.html#:~:text=The%20Health%20Insurance%20Portability%20and,the%20patient's%20consent%20or%20knowledge>): This webpage explains HIPAA standards, which require healthcare providers to protect sensitive patient health information from being disclosed without the patient's consent or knowledge.

Comprehensive Addiction and Recovery Act of 2016 (<https://www.congress.gov/bill/114th-congress/senate-bill/524/text>): This legislation authorizes grant programs designed to expand SUD (especially OUD) prevention, education, treatment, and recovery efforts. The Act includes provisions explicitly aimed at supporting such efforts in communities facing sudden increases in MA use.

Drug Addiction Treatment Act of 2000 (<https://www.congress.gov/bill/106th-congress/house-bill/2634>): This legislation, as amended, allows healthcare professionals who meet certain qualifications to offer FDA-approved narcotic medication treatment for OUD in settings other than opioid treatment programs. (At the time of this publication, buprenorphine is the only approved medication that meets the provisions of the Act.) This is relevant for patients with stimulant use disorder who are also using opioids and wish to initiate buprenorphine treatment. For statutory changes expanding buprenorphine prescribing, see <https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines>.

Fair Sentencing Act of 2010 (<https://www.congress.gov/bill/111th-congress/senate-bill/1789>): This Act reduced the 5- to 10-year “mandatory minimum” prison sentence for possession of low-level crack cocaine. It also removed the mandatory minimum for simple possession of cocaine.

U.S. Department of Justice, Drug Enforcement Administration, Diversion Control Division, Combat Methamphetamine Epidemic Act of 2005 (CMEA) (<https://www.deadiversion.usdoj.gov/meth/index.html>): This webpage interprets CMEA, the federal legislation that bans over-the-counter sales of cold medicines containing ingredients that are commonly used in the manufacture of MA, such as pseudoephedrine. It also limits the amount of these products that can be purchased at one time and tracks purchasers.

21st Century Cures Act: (<https://www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf>): Passed in 2016, this Act was intended to help increase the speed and efficiency of the discovery, development, and delivery of medical cures. It provides U.S. research and healthcare delivery institutions, such as FDA and the National Institutes of Health, with funding to improve clinical trials, enhance data sharing, increase the recruitment of participants in clinical trials, and launch innovative research projects. It also established the State Targeted Response to the Opioid Crisis grant program.

Additional Resources

SAMHSA, Suicide Safe Mobile App (<https://store.samhsa.gov/product/suicide-safe>): Based on SAMHSA's “Suicide Assessment Five-Step Evaluation and Triage” (SAFE-T) card (<https://store.samhsa.gov/product/SAFE-T-Pocket-Card-Suicide-Assessment-Five-Step-Evaluation-and-Triage-for-Clinicians/sma09-4432>), the Suicide Safe mobile app is designed to help providers integrate suicide prevention strategies into their practice and address suicide risk among their patients. The app offers tips on how to communicate effectively with patients and their families, determine appropriate next steps, and make referrals to treatment and community resources. The app is free and can be downloaded from Google Play or the Apple App Store.

American Journal of Psychiatry, Prevalence and Correlates of Prescription Stimulant Use, Misuse, Use Disorders, and Motivations for Misuse Among Adults in the United States (<https://ajp.psychiatryonline.org/doi/10.1176/appi.ajp.2018.17091048>): Published in the April 2018 issue of *The American Journal of Psychiatry*, this article examines data from the 2015 and 2016 releases of the National Survey on Drug Use and Health to establish prevalence rates of prescription stimulant use and misuse, motivations and demographics underlying stimulant misuse, and common sources (other than a legitimate prescription) that users access to acquire stimulants.

Authentic Happiness (<https://www.authentichappiness.sas.upenn.edu>): Authentic Happiness is a University of Pennsylvania website developed by the Positive Psychology Center (<https://ppc.sas.upenn.edu>) to provide free learning resources about Positive Psychology, including readings, videos, research, conferences, questionnaires with feedback, and more. Positive Psychology is the scientific study of the strengths and virtues that enable individuals and communities to thrive.

DHA Solution Delivery Division, T2 Mood Tracker Mobile App: The T2 Mood Tracker mobile app allows users to monitor and track their emotional health. Developed as a tool for service members to record and review their behavior changes, particularly after combat deployments, it has become popular with civilian users, as well. The app allows users to record a range of emotions for anxiety, depression, head injury, stress, posttraumatic stress, and general well-being. An overview of the app is available from the DHA Solution Delivery Division's "Web and Mobile Technology" menu (<https://health.mil/About-MHS/OASDHA/Defense-Health-Agency/Information-Operations-J6/Solution-Delivery-Division>), and the app is available for download from Google Play (<https://play.google.com/store/apps/details?id=com.t2.vas>) or the Apple App Store (<https://apps.apple.com/us/app/t2-mood-tracker/id428373825>).

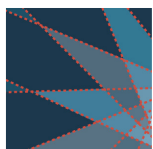
DHA Solution Delivery Division, Virtual Hope Box Mobile App: The Virtual Hope Box mobile app is designed for patients and their behavioral health providers as an accessory to treatment. The app contains simple tools to help patients with coping, relaxation, distraction, and positive thinking. Patients and providers can work together to personalize the app's content on the patient's smartphone according to the patient's specific needs. An overview of the app is available from the DHA Solution Delivery Division's "Web and Mobile Technology" menu (<https://health.mil/About-MHS/OASDHA/Defense-Health-Agency/Information-Operations-J6/Solution-Delivery-Division>), and the app can be downloaded from Google Play (<https://play.google.com/store/apps/details?id=com.t2.vhb&hl=en&gl=US>) or the Apple App Store (<https://apps.apple.com/us/app/virtual-hope-box/id825099621>).

Physician Health Services, Inc., Risks of Stimulant Misuse (<http://www.massmed.org/Physician-Health-Services/Education-and-Resources/Risks-of-Stimulant-Misuse/#.X8VOFUBfw2x>): This webpage discusses the use of prescription stimulants to manage ADHD, along with the clinical and personal reasons that may influence a young person or adult to misuse these drugs.

Psychiatric Times, Issues Pertaining to Misuse of ADHD Prescription Medications (<https://www.psychiatrictimes.com/view/issues-pertaining-misuse-adhd-prescription-medications>): Published in September 2018, this article discusses the use of prescription stimulants to manage ADHD, the characteristics and co-presenting conditions in both young people and adults that may predispose them to substance misuse, and how these factors impact diagnostic and prescribing decisions.

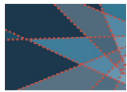
VA, PTSD Coach Mobile App (https://www.ptsd.va.gov/appvid/mobile/ptsdcoach_app.asp#:~:text=PTSD%20Coach%20is%20a%20free%20and%20publicly%20available,is%20not%20intended%20to%20replace%20needed%20professional%20care): The PTSD Coach app can help individuals learn about and manage symptoms that often occur after trauma. Features include reliable information on PTSD and treatments that work, tools for screening and tracking symptoms, convenient, easy-to-use tools to help manage stress symptoms, and direct links to support and help.

This page intentionally left blank.



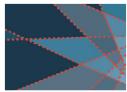
Bibliography

- Abdul-Karim, R., Ryan, C., Rangel, C., & Emmett, M. (2013). Levamisole-induced vasculitis. *Baylor University Medical Center Proceedings*, 26(2), 163–165.
- Abdul-Khabir, W., Hall, T., Swanson, A. N., & Shoptaw, S. (2014). Intimate partner violence and reproductive health among methamphetamine-using women in Los Angeles: A qualitative pilot study. *Journal of Psychoactive Drugs*, 46(4), 310–316.
- Abdul-Quader, A. S., Feelemyer, J., Modi, S., Stein, E. S., Briceno, A., Semaan, S., ... Des Jarlais, D. C. (2013). Effectiveness of structural-level needle/syringe programs to reduce HCV and HIV infection among people who inject drugs: A systematic review. *AIDS and Behavior*, 17(9), 2878–2892.
- A.D.A.M. Medical Encyclopedia. (2021). Rhabdomyolysis. Retrieved May 17, 2021, from <https://medlineplus.gov/ency/article/000473.htm>
- Admon, L. K., Bart, G., Kozhimannil, K. B., Richardson, C. R., Dalton, V. K., & Winkelman, T. (2019). Amphetamine- and opioid-affected births: Incidence, outcomes, and costs, United States, 2004–2015. *American Journal of Public Health*, 109(1), 148–154.
- Agrawal, P. R., Scarabelli, T. M., Saravolatz, L., Kini, A., Jalota, A., Chen-Scarabelli, C., ... Halperin, J. L. (2015). Current strategies in the evaluation and management of cocaine-induced chest pain. *Cardiology in Review*, 23(6), 303–311.
- Aharonovich, E., Hasin, D. S., Nunes, E. V., Stohl, M., Cannizzaro, D., Sarvet, A., ... Genece, K. G. (2018). Modified cognitive behavioral therapy (M-CBT) for cocaine dependence: Development of treatment for cognitively impaired users and results from a Stage 1 trial. *Psychology of Addictive Behaviors*, 32(7), 800–811.
- Ahmad, S. I., Owens, E. B., & Hinshaw, S. P. (2019). Little evidence for late-onset ADHD in a longitudinal sample of women. *Journal of Consulting and Clinical Psychology*, 87(1), 112–117.
- Akwe, J. A. (2017). Pulmonary effects of cocaine use. *Journal of Lung, Pulmonary, and Respiratory Research*, 4(2), 54–58.
- Alexander, P. D., Gicas, K. M., Willi, T. S., Kim, C. N., Boyeva, V., Procyshyn, R. M., ... Barr, A. M. (2017). A comparison of psychotic symptoms in subjects with methamphetamine versus cocaine dependence. *Psychopharmacology*, 234(9–10), 1535–1547.
- Ali, M. M., Nye, E., & West, K. (2020). Substance use disorder treatment, perceived need for treatment, and barriers to treatment among parenting women with substance use disorder in US rural counties. *Journal of Rural Health*. Advance online publication. doi:10.1111/jrh.12488
- Allain, F., Minogianis, E.-A., Roberts, D. C. S., & Samaha, A.-N. (2015). How fast and how often: The pharmacokinetics of drug use are decisive in addiction. *Neuroscience and Biobehavioral Reviews*, 56, 166–179.
- Al-Tayyib, A., Koester, S., Langegger, S., & Raville, L. (2017). Heroin and methamphetamine injection: An emerging drug use pattern. *Substance Use and Misuse*, 52(8), 1051–1058.
- American College of Obstetricians and Gynecologists Committee on Health Care for Underserved Women. (2011). Committee Opinion No. 479: Methamphetamine abuse in women of reproductive age. *Obstetrics and Gynecology*, 117(3), 751–755.
- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.).
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.).
- American Psychological Association. (2008). Sexual orientation & homosexuality. <https://www.apa.org/topics/lgbt/orientation>
- American Psychological Association. (2009). *Report of the APA Task Force on Appropriate Therapeutic Responses to Sexual Orientation*. <https://www.apa.org/pi/lgbt/resources/sexual-orientation>
- American Psychological Association. (2015). Guidelines for psychological practice with transgender and gender nonconforming people. *American Psychologist*, 70(9), 832–864.
- American Society of Addiction Medicine. (2015a). *The ASAM national practice guideline for the use of medications in the treatment of addiction involving opioid use*.
- American Society of Addiction Medicine. (2015b, May 13). What are the ASAM levels of care? <https://www.asamcontinuum.org/knowledgebase/what-are-the-asam-levels-of-care>
- American Society of Addiction Medicine. (2020). The ASAM national practice guideline for the treatment of opioid use disorder: 2020 focused update. *Journal of Addiction Medicine*, 14(2S), 1–91.



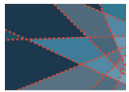
- Anbalagan, S., & Mendez, M. D. (2021). Neonatal abstinence syndrome. In *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK551498/>
- Andermann, A. (2016). Taking action on the social determinants of health in clinical practice: A framework for health professionals. *CMAJ*, 188(17–18), E474–E483.
- Anderson, J. E., Brown, I. E., Olson, K. A., Iverson, K., Cocanour, C. S., & Galante, J. M. (2018). Nonocclusive mesenteric ischemia in patients with methamphetamine use. *Journal of Trauma and Acute Care Surgery*, 84(6), 885–892.
- Anderson, J. L., Adams, C. D., Antman, E. M., Bridges, C. R., Califf, R. M., Casey, Jr., D. E., ... Riegel, B. (2007). ACC/AHA 2007 guidelines for the management of patients with unstable angina/non–ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *Journal of the American College of Cardiology*, 50(7), e1–e157.
- Anderson, K. N., Ailes, E. C., Danielson, M., Lind, J. N., Farr, S. L., Broussard, C. S., & Tinker, S. C. (2018). Attention-deficit/hyperactivity disorder medication prescription claims among privately insured women aged 15–44 years—United States, 2003–2015. *Morbidity and Mortality Weekly Report*, 67(2), 66–70.
- Anderson-Carpenter, K. D., Fletcher, J. B., Swendeman, D., & Reback, C. J. (2019). Associations between sociodemographic characteristics and substance use disorder severity among methamphetamine-using men who have sex with men. *Substance Use and Misuse*, 54(11), 1763–1773.
- Andrade, C. (2018). Risk of major congenital malformations associated with the use of methylphenidate or amphetamines in pregnancy. *Journal of Clinical Psychiatry*, 79(1), 18f12108.
- Anker, A. L., & Crowley, T. J. (1982). Use of contingency contracts in specialty clinics for cocaine abuse. *NIDA Research Monograph*, 41, 452–459.
- Arkowitz, H., Miller, W. R., & Rollnick, S. (Eds.). (2015). *Motivational interviewing in the treatment of psychological problems*. Guilford Press.
- Armenian, P., Effron, Z., Garbi, N., Dirks, R., Benowitz, N. L., & Gerona, R. R. (2019). Stimulant drugs are associated with violent and penetrating trauma. *American Journal of Emergency Medicine*, 37(4), 645–650.
- Arria, A. M., & DuPont, R. L. (2018). Prescription stimulant use and misuse: Implications for responsible prescribing practices. *American Journal of Psychiatry*, 175(8), 707–708.
- ARUP Laboratories. (2019). Drug plasma half-life and urine detection windows.
- AshaRani, P. V., Hombali, A., Seow, E., Ong, W. J., Tan, J. H., & Subramaniam, M. (2020). Non-pharmacological interventions for methamphetamine use disorder: A systematic review. *Drug and Alcohol Dependence*, 212, 108060.
- Ashok, A. H., Mizuno, Y., Volkow, N. D., & Howes, O. D. (2017). Association of stimulant use with dopaminergic alterations in users of cocaine, amphetamine, or methamphetamine: A systematic review and meta-analysis. *JAMA Psychiatry*, 74(5), 511–519.
- Asser, A., & Taba, P. (2015). Psychostimulants and movement disorders. *Frontiers in Neurology*, 6, 75.
- Attaran, H. (2017). Fatal small intestinal ischemia due to methamphetamine intoxication: Report of a case with autopsy results. *Acta Medica Iranica*, 55(5), 344–347.
- Bachi, K., Mani, V., Jeyachandran, D., Fayad, Z. A., Goldstein, R. Z., & Alia-Klein, N. (2017). Vascular disease in cocaine addiction. *Atherosclerosis*, 262, 154–162.
- Bahdila, D., Aldosari, M., Abdullah, A., Nelson, J. L., Hegazi, F., Badamia, R., ... Agaku, I. T. (2020). Cocaine, polysubstance abuse, and oral health outcomes, NHANES 2009 to 2014. *Journal of Periodontology*. Advance online publication. doi:10.1002/JPER.19-0509
- Bailey, Z. D., Krieger, N., Agénor, M., Graves, J., Linos, N., & Bassett, M. T. (2017). Structural racism and health inequities in the USA: Evidence and interventions. *Lancet*, 389(10077), 1453–1463.
- Baldwin, J. A., Eaves, E. R., Brown, B. G., Elwell, K., & Williamson, H. J. (2020). The behavioral health of American Indian/Alaska Native populations: Risk and resiliency. In B. L. Levin & A. Hanson (Eds.), *Foundations of behavioral health* (pp. 205–230). Springer.
- Baldwin, J. A., Johnson, J. L., & Benally, C. C. (2009). Building partnerships between indigenous communities and universities: Lessons learned in HIV/AIDS and substance abuse prevention research. *American Journal of Public Health*, 99(Suppl. 1), S77–S82.
- Ballester, J., Valentine, G., & Sofuoglu, M. (2017). Pharmacological treatments for methamphetamine addiction: Current status and future directions. *Expert Review of Clinical Pharmacology*, 10(3), 305–314.
- Balsam, K. F., Huang, B., Fieland, K. C., Simoni, J. M., & Walters, K. L. (2004). Culture, trauma, and wellness: A comparison of heterosexual and lesbian, gay, bisexual, and two-spirit Native Americans. *Cultural Diversity and Ethnic Minority Psychology*, 10(3), 287–301.
- Baltes, A., Akhtar, W., Birstler, J., Olson-Streed, H., Eagen, K., Seal, D., ... Brown, R. (2020). Predictors of skin and soft tissue infections among sample of rural residents who inject drugs. *Harm Reduction Journal*, 17(1), 96.
- Baradhi, K. M., Pathireddy, S., Bose, S., & Aeddula, N. R. (2019). Methamphetamine (N-methylamphetamine)-induced renal disease: Underevaluated cause of end-stage renal disease (ESRD). *BMJ Case Reports*, 12(9), e230288.
- Baral, S. D., Poteat, T., Strömdahl, S., Wirtz, A. L., Guadamuz, T. E., & Beyrer, C. (2013). Worldwide burden of HIV in transgender women: A systematic review and meta-analysis. *Lancet: Infectious Diseases*, 13(3), 214–222.

- Barker, S. L., & Maguire, N. (2017). Experts by experience: Peer support and its use with the homeless. *Community Mental Health Journal*, 53(5), 598–612.
- Barrenger, S. L., Hamovitch, E. K., & Rothman, M. R. (2019). Enacting lived experiences: Peer specialists with criminal justice histories. *Psychiatric Rehabilitation Journal*, 42(1), 9–16.
- Barry, C. L., Martin, A., & Busch, S. H. (2012). ADHD medication use following FDA risk warnings. *Journal of Mental Health Policy and Economics*, 15(3), 119–125.
- Bashshur, R. L., Shannon, G. W., Bashshur, N., & Yellowlees, P. M. (2016). The empirical evidence for telemedicine interventions in mental disorders. *Telemedicine Journal and E-Health*, 22(2), 87–113.
- Bassuk, E. L., Hanson, J., Greene, R. N., Richard, M., & Laudet, A. (2016). Peer-delivered recovery support services for addictions in the United States: A systematic review. *Journal of Substance Abuse Treatment*, 63, 1–9.
- Batchelder, A. W., Safren, S., Mitchell, A. D., Ivardic, I., & O’Cleirigh, C. (2017). Mental health in 2020 for men who have sex with men in the United States. *Sexual Health*, 14(1), 59–71.
- Bauermeister, J. A., Eaton, L., Meanley, S., & Pingel, E. S., on behalf of the UHIP Partnership. (2017). Transactional sex with regular and casual partners among young men who have sex with men in the Detroit metro area. *American Journal of Men’s Health*, 11(3), 498–507.
- Baxter, A. J., Tweed, E. J., Katikireddi, S. V., & Thomson, H. (2019). Effects of Housing First approaches on health and well-being of adults who are homeless or at risk of homelessness: Systematic review and meta-analysis of randomised controlled trials. *Journal of Epidemiology and Community Health*, 73(5), 379–387.
- Beard, C., Hsu, K. J., Rifkin, L. S., Busch, A. B., & Björgvinsson, T. (2016). Validation of the PHQ-9 in a psychiatric sample. *Journal of Affective Disorders*, 193, 267–273.
- Beiter, R. M., Peterson, A. B., Abel, J., & Lynch, W. J. (2016). Exercise during early, but not late abstinence, attenuates subsequent relapse vulnerability in a rat model. *Translational Psychiatry*, 6(4), e792.
- Bekkering, G. E., Mariën, D., Parylo, O., & Hannes, K. (2016). The effectiveness of self-help groups for adolescent substance misuse: A systematic review. *Journal of Child and Adolescent Substance Abuse*, 25(3), 229–244.
- Benishek, L. A., Dugosh, K. L., Kirby, K. C., Matejkowski, J., Clements, N. T., Seymour, B. L., & Festinger, D. S. (2014). Prize-based contingency management for the treatment of substance abusers: A meta-analysis. *Addiction*, 109(9), 1426–1436.
- Benotsch, E. G., Zimmerman, R., Cathers, L., McNulty, S., Pierce, J., Heck, T., ... Snipes, D. (2013). Non-medical use of prescription drugs, polysubstance use, and mental health in transgender adults. *Drug and Alcohol Dependence*, 132(1–2), 391–394.
- Benson, K., Flory, K., Humphreys, K. L., & Lee, S. S. (2015). Misuse of stimulant medication among college students: A comprehensive review and meta-analysis. *Clinical Child and Family Psychology Review*, 18(1), 50–76.
- Bentley, K. H., Sakurai, H., Lowman, K. L., Rines-Toth, L., McKowen, J., Pedrelli, P., ... Yule, A. M. (2021). Validation of brief screening measures for depression and anxiety in young people with substance use disorders. *Journal of Affective Disorders*, 282, 1021–1029.
- Berenz, E. C., & Coffey, S. F. (2012). Treatment of co-occurring posttraumatic stress disorder and substance use disorders. *Current Psychiatry Reports*, 14(5), 469–477.
- Berridge, K. C., & Kringelbach, M. L. (2015). Pleasure systems in the brain. *Neuron*, 86(3), 646–664.
- Berry, M. S., Bruner, N. R., Herrmann, E. S., Johnson, P. S., & Johnson, M. W. (2020). Methamphetamine administration dose effects on sexual desire, sexual decision making, and delay discounting. *Experimental and Clinical Psychopharmacology*. Advance online publication. doi:10.1037/pha0000398
- Bhide, A., Shah, P. S., & Acharya, G. (2018). A simplified guide to randomized controlled trials. *Acta Obstetrica et Gynecologica Scandinavica*, 97(4), 380–387.
- Bhuvaneswar, C. G., Chang, G., Epstein, L. A., & Stern, T. A. (2008). Cocaine and opioid use during pregnancy: Prevalence and management. *Primary Care Companion to the Journal of Clinical Psychiatry*, 10(1), 59–65.
- Black, D. S., & Amaro, H. (2019). Moment-by-Moment in Women’s Recovery (MMWR): Mindfulness-based intervention effects on residential substance use disorder treatment retention in a randomized controlled trial. *Behaviour Research and Therapy*, 120, 103437.
- Black, J. C., Bau, G. E., Iwanicki, J. L., & Dart, R. C. (2021, February 2). Association of medical stimulants with mortality in the US from 2010 to 2017. *JAMA Internal Medicine*, 181(5):707–709.
- Blanco, C., Compton, W. M., Saha, T. D., Goldstein, B. I., Ruan, W. J., Huang, B., & Grant, B. F. (2017). Epidemiology of DSM-5 bipolar I disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions–III. *Journal of Psychiatric Research*, 84, 310–317.
- Blanco, C., Okuda, M., Markowitz, J. C., Liu, S. M., Grant, B. F., & Hasin, D. S. (2010). The epidemiology of chronic major depressive disorder and dysthymic disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Clinical Psychiatry*, 71(12), 1645–1656.



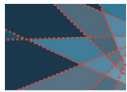
- Blevins, C. A., Weathers, F. W., Davis, M. T., Witte, T. K., & Domino, J. L. (2015). The posttraumatic stress disorder checklist for DSM-5 (PCL-5): Development and initial psychometric evaluation. *Journal of Traumatic Stress, 28*(6), 489–498.
- Blonigen, D. M., Finney, J. W., Wilbourne, P. L., & Moos, R. H. (2015). Psychosocial treatments for substance use disorders. In P. E. Nathan & J. M. Gorman (Eds.), *A guide to treatments that work* (pp. 731–761). Oxford University Press.
- Board, A. R., Guy, G., Jones, C. M., & Hoots, B. (2020). Trends in stimulant dispensing by age, sex, state of residence, and prescriber specialty—United States, 2014–2019. *Drug and Alcohol Dependence, 217*, 108297.
- Bohnert, K. M., Ilgen, M. A., Louzon, S., McCarthy, J. F., & Katz, I. R. (2017). Substance use disorders and the risk of suicide mortality among men and women in the US Veterans Health Administration. *Addiction, 112*(7), 1193–1201.
- Boileau, I., McCluskey, T., Tong, J., Furukawa, Y., Houle, S., & Kish, S. J. (2016). Rapid recovery of vesicular dopamine levels in methamphetamine users in early abstinence. *Neuropsychopharmacology, 41*(4), 1179–1187.
- Bolloni, C., Badas, P., Corona, G., & Diana, M. (2018). Transcranial magnetic stimulation for the treatment of cocaine addiction: Evidence to date. *Substance Abuse and Rehabilitation, 9*, 11–21.
- Bond Edmond, M., Aletraris, L., & Roman, P. M. (2015). Rural substance use treatment centers in the United States: An assessment of treatment quality by location. *American Journal of Drug and Alcohol Abuse, 41*(5), 449–457.
- Bourne, A., & Weatherburn, P. (2017). Substance use among men who have sex with men: Patterns, motivations, impacts and intervention development need. *Sexually Transmitted Infections, 93*(5), 342–346.
- Bramness, J. G., Gundersen, Ø. H., Guterstam, J., Rognli, E. B., Konstenius, M., Løberg, E. M., ... Franck, J. (2012). Amphetamine-induced psychosis—A separate diagnostic entity or primary psychosis triggered in the vulnerable? *BMC Psychiatry, 12*, 221.
- Bramness, J. G., & Rognli, E. B. (2016). Psychosis induced by amphetamines. *Current Opinion in Psychiatry, 29*(4), 236–241.
- Bramson, H., Des Jarlais, D. C., Arasteh, K., Nugent, A., Guardino, V., Feelemyer, J., & Hodel, D. (2015). State laws, syringe exchange, and HIV among persons who inject drugs in the United States: History and effectiveness. *Journal of Public Health Policy, 36*(2), 212–230.
- Braunwarth, W.-D., Christ, M., Dirks, H., Dyba, J., Härtel-Petri, R., Harfst, T., ... Krampe-Scheidler, A. (2016). *S3 practice guideline: Methamphetamine-related disorders*. Ärztliche Zentrum für Qualität in der Medizin.
- Brecht, M. L., & Herbeck, D. (2013). Methamphetamine use and violent behavior: User perceptions and predictors. *Journal of Drug Issues, 43*(4), 468–482.
- Brecht, M. L., & Herbeck, D. (2014). Time to relapse following treatment for methamphetamine use: A long-term perspective on patterns and predictors. *Drug and Alcohol Dependence, 139*(1), 18–25.
- Brewer, J. A., Elwafi, H. M., & Davis, J. H. (2013). Craving to quit: Psychological models and neurobiological mechanisms of mindfulness training as treatment for addictions. *Psychology of Addictive Behaviors, 27*(2), 366–379.
- Brinkley-Rubinstein, L. (2015). Understanding the effects of multiple stigmas among formerly incarcerated HIV-positive African American men. *AIDS Education and Prevention, 27*(2), 167–179.
- British Columbia Center for Disease Control. (2011). Acidifier (ascorbic acid) and injection drug use: Questions and answers.
- Bromberg-Martin, E. S., Matsumoto, M., & Hikosaka, O. (2010). Dopamine in motivational control: Rewarding, aversive, and alerting. *Neuron, 68*(5), 815–834.
- Bronson, J., Stroop, J., Zimmer, S., & Berzofsky, M. (2017). *Drug use, dependence, and abuse among state prisoners and jail inmates, 2007–2009* (NCJ 250546). U.S. Department of Justice, Bureau of Justice Statistics.
- Brooks, R. A., Landovitz, R. J., Kaplan, R. L., Lieber, E., Lee, S. J., & Barkley, T. W. (2012). Sexual risk behaviors and acceptability of HIV pre-exposure prophylaxis among HIV-negative gay and bisexual men in serodiscordant relationships: A mixed methods study. *AIDS Patient Care and STDs, 26*(2), 87–94.
- Brown, H. D., & DeFulio, A. (2020). Contingency management for the treatment of methamphetamine use disorder: A systematic review. *Drug and Alcohol Dependence, 216*, 108307.
- Brown, R. A., Dickerson, D. L., & D'Amico, E. J. (2016). Cultural identity among urban American Indian/Alaska Native youth: Implications for alcohol and drug use. *Prevention Science, 17*(7), 852–861.
- Browne, T., Priester, M. A., Clone, S., Iachini, A., DeHart, D., & Hock, R. (2016). Barriers and facilitators to substance use treatment in the rural South: A qualitative study. *Journal of Rural Health, 32*(1), 92–101.
- Brucoleri, R. E., & Burns, M. M. (2016). A literature review of the use of sodium bicarbonate for the treatment of QRS widening. *Journal of Medical Toxicology, 12*(1), 121–129.
- Bruggisser, M., Bodmer, M., & Liechti, M. E. (2011). Severe toxicity due to injected but not oral or nasal abuse of methylphenidate tablets. *Swiss Medical Weekly, 141*, w13267.

- Buck, S. A., Torregrossa, M. M., Logan, R. W., & Freyberg, Z. (2021). Roles of dopamine and glutamate co-release in the nucleus accumbens in mediating the actions of drugs of abuse. *FEBS Journal*, 288(5), 1462–1474.
- Burch, A. E., Rash, C. J., & Petry, N. M. (2017). Cocaine-using substance abuse treatment patients with and without HIV respond well to contingency management treatment. *Journal of Substance Abuse Treatment*, 77, 21–25.
- Bureau of Justice Statistics. (2020). *Data collected under the First Step Act, 2019* (NCJ 254268). U.S. Department of Justice, Office of Justice Programs.
- Butler, A. J., Rehm, J., & Fischer, B. (2017). Health outcomes associated with crack-cocaine use: Systematic review and meta-analyses. *Drug and Alcohol Dependence*, 180, 401–416.
- Cachay, E. R., Moini, N., Kosakovsky Pond, S. L., Pesano, R., Lie, Y. S., Aiem, H., ... Smith, D. M. (2007). Active methamphetamine use is associated with transmitted drug resistance to non-nucleoside reverse transcriptase inhibitors in individuals with HIV infection of unknown duration. *Open AIDS Journal*, 1, 5–10.
- Cain, M. A., Bornick, P., & Whiteman, V. (2013). The maternal, fetal, and neonatal effects of cocaine exposure in pregnancy. *Clinical Obstetrics and Gynecology*, 56(1), 124–132.
- California Correctional Health Care Services. (2020). *CCHCS care guide: Intoxication and withdrawal*.
- Calsyn, D. A., Cousins, S. J., Hatch-Maillette, M. A., Forcehimes, A., Mandler, R., Doyle, S. R., & Woody, G. (2010). Sex under the influence of drugs or alcohol: Common for men in substance abuse treatment and associated with high-risk sexual behavior. *American Journal on Addictions*, 19(2), 119–127.
- Campbell, A. N. C., Nunes, E. V., Matthews, A. G., Stitzer, M., Miele, G. M., Polsky, D., ... Ghitza, U. E. (2014). Internet-delivered treatment for substance abuse: A multisite randomized controlled trial. *American Journal of Psychiatry*, 171, 683–690.
- Cantrell, F. L., Ogera, P., Mallett, P., & McIntyre, I. M. (2014). Fatal oral methylphenidate intoxication with postmortem concentrations. *Journal of Forensic Sciences*, 59(3), 847–849.
- Carlin, N., Nguyen, N., & DePasquale, J. R. (2014). Multiple gastrointestinal complications of crack cocaine abuse. *Case Reports in Medicine*, 2014, 512939.
- Carmack, S. A., Koob, G. F., & Anagnostaras, S. G. (2017). Learning and memory in addiction. In J. H. Byrne (Ed.), *Learning and memory: A comprehensive reference* (2nd ed., pp. 523–538). Elsevier.
- Carrico, A. W., Flentje, A., Kober, K., Lee, S., Hunt, P., Riley, E. D., ... Aouizerat, B. E. (2018). Recent stimulant use and leukocyte gene expression in methamphetamine users with treated HIV infection. *Brain, Behavior, and Immunity*, 71, 108–115.
- Carrico, A. W., Hunt, P. W., Neilands, T. B., Dilworth, S. E., Martin, J. N., Deeks, S. G., & Riley, E. D. (2019). Stimulant use and viral suppression in the era of universal antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes*, 80(1), 89–93.
- Carrico, A. W., Neilands, T. B., Dilworth, S. E., Evans, J. L., Gómez, W., Jain, J. P., ... Moskowitz, J. T. (2019). Randomized controlled trial of a positive affect intervention to reduce HIV viral load among sexual minority men who use methamphetamine. *Journal of the International AIDS Society*, 22(12), e25436.
- Carrico, A. W., Shoptaw, S., Cox, C., Stall, R., Li, X., Ostrow, D. G., ... Plankey, M. W. (2014). Stimulant use and progression to AIDS or mortality after the initiation of highly active anti-retroviral therapy. *Journal of Acquired Immune Deficiency Syndromes*, 67(5), 508–513.
- Carroll, K. M., Nich, C., Petry, N. M., Eagan, D. A., Shi, J. M., & Ball, S. A. (2016). A randomized factorial trial of disulfiram and contingency management to enhance cognitive behavioral therapy for cocaine dependence. *Drug and Alcohol Dependence*, 160(1), 135–142.
- Carroll, K. M., Nich, C., Shi, J. M., Eagan, D., & Ball, S. A. (2012). Efficacy of disulfiram and Twelve Step facilitation in cocaine-dependent individuals maintained on methadone: A randomized placebo-controlled trial. *Drug and Alcohol Dependence*, 126(1–2), 224–231.
- Carroll, K. M., Rounsaville, B. J., & Gawin, F. H. (1991). A comparative trial of psychotherapies for ambulatory cocaine abusers: Relapse prevention and interpersonal psychotherapy. *American Journal of Drug and Alcohol Abuse*, 17, 229–247.
- Carroll, K. M., Rounsaville, B. J., Gordon, L. T., Nich, C., Jatlow, P., Bisighini, R. M., & Gawin, F. H. (1994). Psychotherapy and pharmacotherapy for ambulatory cocaine abusers. *Archives of General Psychiatry*, 51, 177–187.
- Carroll, K. M., Rounsaville, B. J., & Keller, D. S. (1991). Relapse prevention strategies for the treatment of cocaine abusers. *American Journal of Drug and Alcohol Abuse*, 17, 249–265.
- Carroll, K. M., Rounsaville, B. J., Nich, C., Gordon, L. T., Wirtz, P. W., & Gawin, F. (1994). One-year followup of psychotherapy and pharmacotherapy for cocaine dependence. *Archives of General Psychiatry*, 51, 989–997.
- Carson, E. A. (2020). *Prisoners in 2019* (NCJ 255115). U.S. Department of Justice.
- Castillo-Mancilla, J. R., Brown, T. T., Erlandson, K. M., Palella, Jr., F. J., Gardner, E. M., Macatangay, B. J. C., ... Wada, N. I. (2016). Suboptimal adherence to combination antiretroviral therapy is associated with higher levels of inflammation despite HIV suppression. *Clinical Infectious Diseases*, 63(12), 1661–1667.



- Center for Behavioral Health Statistics and Quality. (2016). *Results from the 2015 National Survey on Drug Use and Health: Detailed tables*. Substance Abuse and Mental Health Services Administration.
- Center for Behavioral Health Statistics and Quality. (2017). *Treatment Episode Data Set (TEDS): 2005–2015. National admissions to substance abuse treatment services*. BHSIS Series S-91, HHS Publication No. (SMA) 17-5037. Substance Abuse and Mental Health Services Administration.
- Center for Behavioral Health Statistics and Quality. (2019). *Treatment Episode Data Set (TEDS): 2017—Admissions to and discharges from publicly-funded substance use treatment*. Substance Abuse and Mental Health Services Administration.
- Center for Behavioral Health Statistics and Quality. (2020a). *Results from the 2019 National Survey on Drug Use and Health: Detailed tables*. Substance Abuse and Mental Health Services Administration. <https://www.samhsa.gov/data/>
- Center for Behavioral Health Statistics and Quality. (2020b). *Treatment Episode Data Set (TEDS). Based on administrative data reported by states to TEDS through July 1, 2020*. Substance Abuse and Mental Health Services Administration. <https://www.dasis.samhsa.gov/webt/newmapv1.htm#>
- Center for Integrated Healthcare. (2013). *Cocaine. Information for behavioral health providers in primary care*. U.S. Department of Veterans Affairs.
- Center for Substance Abuse Treatment. (2000). *Integrating substance abuse treatment and vocational services*. Treatment Improvement Protocol (TIP) Series 38. HHS Publication No. (SMA) 12-4216. Substance Abuse and Mental Health Services Administration.
- Center for Substance Abuse Treatment. (2005). *Substance abuse treatment for adults in the criminal justice system*. Treatment Improvement Protocol (TIP) Series 44. HHS Publication No. (SMA) 13-4056. Substance Abuse and Mental Health Services Administration.
- Center for Substance Abuse Treatment. (2006). *Counselor's treatment manual: Matrix intensive outpatient treatment for people with stimulant use disorders*. HHS Publication No. (SMA) 13-4152. Substance Abuse and Mental Health Services Administration.
- Center for Substance Abuse Treatment. (2012). *A provider's introduction to substance abuse treatment for lesbian, gay, bisexual, and transgender individuals*. HHS Publication No. (SMA) 12-4104. Substance Abuse and Mental Health Services Administration.
- Centers for Disease Control and Prevention. (n.d.-a). About opioid use during pregnancy. <https://www.cdc.gov/pregnancy/opioids/basics.html>
- Centers for Disease Control and Prevention. (n.d.-b). Estimated per-act probability of acquiring HIV from an infected source, by exposure act. <https://www.cdc.gov/hiv/risk/estimates/riskbehaviors.html>
- Centers for Disease Control and Prevention. (n.d.-c). Frequently asked questions: Hepatitis A outbreaks. <https://www.cdc.gov/hepatitis/outbreaks/FAQs-HepAOutbreaks.htm>
- Centers for Disease Control and Prevention. (n.d.-d). Pregnancy and oral health. <https://www.cdc.gov/oralhealth/publications/features/pregnancy-and-oral-health.html>
- Centers for Disease Control and Prevention. (n.d.-e). *Prevent bacterial and fungal infections in patients who inject drugs*. U.S. Department of Health and Human Services.
- Centers for Disease Control and Prevention. (n.d.-f). Syringe services programs (SSPs) FAQs. <https://www.cdc.gov/ssp/syringe-services-programs-faq.html>
- Centers for Disease Control and Prevention. (n.d.-g). What is viral hepatitis? <https://www.cdc.gov/hepatitis/abc/index.htm>
- Centers for Disease Control and Prevention. (2011). *Hepatitis C virus infection among adolescents and young adults: Massachusetts, 2002-2009. Morbidity and Mortality Weekly Report*, 60(17), 537–541.
- Centers for Disease Control and Prevention. (2014). *HIV and young men who have sex with men*. U.S. Department of Health and Human Services.
- Centers for Disease Control and Prevention. (2015). *Epidemiology and prevention of vaccine-preventable diseases* (13th ed.). Public Health Foundation.
- Centers for Disease Control and Prevention. (2016). *Proven HIV prevention methods* [Fact sheet]. U.S. Department of Health and Human Services. <https://www.cdc.gov/nchhstp/newsroom/docs/factsheets/HIV-Proven-Prevention-Methods-508.pdf>
- Centers for Disease Control and Prevention. (2018, April 16). Surveillance for viral hepatitis—United States, 2016. <https://www.cdc.gov/hepatitis/statistics/2016surveillance/commentary.htm>
- Centers for Disease Control and Prevention. (2019). *Annual surveillance report of drug-related risks and outcomes—United States, 2019*. U.S. Department of Health and Human Services.
- Centers for Disease Control and Prevention. (2020a, May 26). What can decrease HIV risk? <https://hivrisk.cdc.gov/can-decrease-hiv-risk/>
- Centers for Disease Control and Prevention. (2020b, August 18). People experiencing homelessness and viral hepatitis. <https://www.cdc.gov/hepatitis/populations/peh.htm>

- Centers for Disease Control and Prevention. (2020c, December 17). CDC Health Advisory: *Increase in fatal drug overdoses across the United States driven by synthetic opioids before and during the COVID-19 pandemic* (CDCHAN-00438). <https://emergency.cdc.gov/han/2020/han00438.asp>
- Centers for Disease Control and Prevention. (2021a). *Estimated HIV incidence and prevalence in the United States, 2015–2019*. (HIV Surveillance Supplemental Report, 26 [No. 1]).
- Centers for Disease Control and Prevention. (2021b). HIV and people who inject drugs. <https://www.cdc.gov/hiv/group/hiv-idu.html>
- Centers for Disease Control and Prevention. (2021c). Viral hepatitis surveillance report 2019: Hepatitis A. <https://www.cdc.gov/hepatitis/statistics/2019surveillance/HepA.htm>
- Centers for Disease Control and Prevention. (2021d). Viral hepatitis surveillance report 2019 – Introduction. <https://www.cdc.gov/hepatitis/statistics/2019surveillance/Introduction.htm>
- Centers for Disease Control and Prevention. (2021e, March 29). Widespread person-to-person outbreaks of hepatitis A across the United States. <https://www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm>
- Centers for Medicare & Medicaid Services. (2016). *Drug diversion: What is a prescriber's role in preventing the diversion of prescription drugs?* U.S. Department of Health and Human Services.
- Cepeda, J. A., Vickerman, P., Bruneau, J., Zang, G., Borquez, A., Farrell, M., ... Martin, N. K. (2020). Estimating the contribution of stimulant injection to HIV and HCV epidemics among people who inject drugs and implications for harm reduction: A modeling analysis. *Drug and Alcohol Dependence*, 213, 108135.
- Charnigo, R., Noar, S. M., Garnett, C., Crosby, R., Palmgreen, P., & Zimmerman, R. S. (2013). Sensation seeking and impulsivity: Combined associations with risky sexual behavior in a large sample of young adults. *Journal of Sex Research*, 50(5), 480–488.
- Chartier, K. G., Carmody, T., Akhtar, M., Stebbins, M. B., Walters, S. T., & Warden, D. (2015). Hispanic subgroups, acculturation, and substance abuse treatment outcomes. *Journal of Substance Abuse Treatment*, 59, 74–82.
- Chen, H.-Y., Albertson, T. E., & Olson, K. R. (2016). Treatment of drug-induced seizures. *British Journal of Clinical Pharmacology*, 81(3), 412–419.
- Chen, J., Feeney, E., & Chung, R. (2014). HCV and HIV co-infection: Mechanisms and management. *Nature Reviews Gastroenterology and Hepatology*, 11(6), 362–371.
- Chen, L. Y., Crum, R. M., Strain, E. C., Alexander, G. C., Kaufmann, C., & Mojtabai, R. (2016). Prescriptions, nonmedical use, and emergency department visits involving prescription stimulants. *Journal of Clinical Psychiatry*, 77(3), e297–e304.
- Cheng, W. S., Garfein, R. S., Semple, S. J., Strathdee, S. A., Zians, J. K., & Patterson, T. L. (2010). Binge use and sex and drug use behaviors among HIV(-), heterosexual methamphetamine users in San Diego. *Substance Use and Misuse*, 45(1–2), 116–133.
- Chermack, S. T., Bonar, E. E., Goldstick, J. E., Winters, J., Blow, F. C., Friday, S., ... Walton, M. A. (2019). A randomized controlled trial for aggression and substance use involvement among veterans: Impact of combining motivational interviewing, cognitive behavioral treatment and telephone-based continuing care. *Journal of Substance Abuse Treatment*, 98, 78–88.
- Chermack, S. T., Grogan-Kaylor, A., Perron, B. E., Murray, R. L., De Chavez, P., & Walton, M. A. (2010). Violence among men and women in substance use disorder treatment: A multi-level event-based analysis. *Drug and Alcohol Dependence*, 112(3), 194–200.
- Chettiar, J., Shannon, K., Wood, E., Zhang, R., & Kerr, T. (2010). Survival sex work involvement among street-involved youth who use drugs in a Canadian setting. *Journal of Public Health (Oxford, England)*, 32(3), 322–327.
- Chiesa, A., & Serretti, A. (2014). Are mindfulness-based interventions effective for substance use disorders? A systematic review of the evidence. *Substance Use and Misuse*, 49(5), 492–512.
- Childress, A. C., Komolova, M., & Sallee, F. R. (2019). An update on the pharmacokinetic considerations in the treatment of ADHD with long-acting methylphenidate and amphetamine formulations. *Expert Opinion on Drug Metabolism and Toxicology*, 15(11), 937–974.
- Childress, A. R., Mozley, P. D., McElgin, W., Fitzgerald, J., Reivich, M., & O'Brien, C. P. (1999). Limbic activation during cue-induced cocaine craving. *American Journal of Psychiatry*, 156(1), 11–18.
- Chin, J. M., & Bartholomew, M. L. (2020). Methamphetamine use in pregnant women in Hawai'i: A case series. *Hawai'i Journal of Health and Social Welfare*, 79(5 Suppl. 1), 40–43.
- Chiu, V. M., & Schenk, J. O. (2012). Mechanism of action of methamphetamine within the catecholamine and serotonin areas of the central nervous system. *Current Drug Abuse Reviews*, 5(3), 227–242.
- Choi, K., Imrie, A., Lourie, R., & Cross, T. (2019). Intestinal ischemia due to methamphetamine use: A case report. *International Journal of Surgery Case Reports*, 58, 11–13.



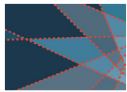
- Chou, R., Korthuis, P. T., McCarty, D., Coffin, P., Griffin, J., Davis-O'Reilly, C., ... Daya, M. (2017). *Management of suspected opioid overdose with naloxone by emergency medical services personnel* (AHRQ Publication No. 17-EHC025-EF). Agency for Healthcare Research and Quality.
- Christine, C. W., Garwood, E. R., Schrock, L. E., Austin, D. E., & McCulloch, C. E. (2010). Parkinsonism in patients with a history of amphetamine exposure. *Movement Disorders*, 25(2), 228–231.
- Ciccarone, D. (2011). Stimulant abuse: Pharmacology, cocaine, methamphetamine, treatment, attempts at pharmacotherapy. *Primary Care: Clinics in Office Practice*, 38(1), 41–58.
- Ciccarone, D., & Harris, M. (2015). Fire in the vein: Heroin acidity and its proximal effect on users' health. *International Journal on Drug Policy*, 26(11), 1103–1110.
- Clague, J., Belin, T. R., & Shetty, V. (2017). Mechanisms underlying methamphetamine-related dental disease. *Journal of the American Dental Association*, 148(6), 377–386.
- Clarke, K., Harris, D., Zweifler, J. A., Lasher, M., Mortimer, R. B., & Hughes, S. (2016). The significance of harm reduction as a social and health care intervention for injecting drug users: An exploratory study of a needle exchange program in Fresno, California. *Social Work in Public Health*, 31(5), 398–407.
- Clary, E., Ribar, C., & Weigensberg, E. (2020). *Challenges in providing substance use disorder treatment to child welfare clients in rural communities*. U.S. Department of Health and Human Services, Office of the Assistant Secretary for Planning and Evaluation.
- Clemow, D. B., & Walker, D. J. (2014). The potential for misuse and abuse of medications in ADHD: A review. *Postgraduate Medicine*, 126(5), 64–81.
- Closson, E. F., Mitty, J. A., Malone, J., Mayer, K. H., & Mimiaga, M. J. (2018). Exploring strategies for PrEP adherence and dosing preferences in the context of sexualized recreational drug use among MSM: A qualitative study. *AIDS Care*, 30(2), 191–198.
- Cockroft, J. D., Adams, S. M., Bonnet, K., Matlock, D., McMillan, J., & Schlundt, D. (2019). "A scarlet letter": Stigma and other factors affecting trust in the health care system for women seeking substance abuse treatment in a community setting. *Substance Abuse*, 40(2), 170–177.
- Coe, M. A., Jufer Phipps, R. A., Cone, E. J., & Walsh, S. L. (2018). Bioavailability and pharmacokinetics of oral cocaine in humans. *Journal of Analytical Toxicology*, 42(5), 285–292.
- Colaneri, N., Keim, S., & Adesman, A. (2017). Physician practices to prevent ADHD stimulant diversion and misuse. *Journal of Substance Abuse Treatment*, 74, 26–34.
- Cole, C., Jones, L., McVeigh, J., Kicman, A., Syed, Q., & Bellis, M. A. (2010). *CUT: A guide to adulterants, bulking agents, and other contaminants found in illicit drugs*. Liverpool John Moores University, Faculty of Health and Applied Social Sciences, Centre for Public Health.
- Coleman, E., Bockting, W., Botzer, M., Cohen-Kettenis, P., DeCuypere, G., Feldman, J., ... Zucker, K. (2012). *Standards of care for the health of transsexual, transgender, and gender-nonconforming people*. World Professional Association for Transgender Health.
- Colledge, S., Larney, S., Bruno, R., Gibbs, D., Degenhardt, L., Yuen, W. S., ... Peacock, A. (2020). Profile and correlates of injecting-related injuries and diseases among people who inject drugs in Australia. *Drug and Alcohol Dependence*, 216, 108267.
- Compton, W. M., Han, B., Blanco, C., Johnson, K., & Jones, C. M. (2018). Prevalence and correlates of prescription stimulant use, misuse, use disorders, and motivations for misuse among adults in the United States. *American Journal of Psychiatry*, 175(8), 741–755.
- Conner, K. O. (2020). *Exploring the intersections of historical trauma and race in criminal justice and behavioral health*. [Handout showing PowerPoint slides]. <https://www.usf.edu/cbcs/mhlp/tac/documents/florida-main/cjmhsa-tac-quarterly-conf-calls/conner-intersection-of-historical-trauma-race-bh-cj-august-2020.pdf>
- Connolly, D., & Gilchrist, G. (2020). Prevalence and correlates of substance use among transgender adults: A systematic review. *Addictive Behaviors*, 111, 106544.
- Cook, J., Lloyd-Jones, M., Arunogiri, S., Ogden, E., & Bonomo, Y. (2017). Managing attention deficit hyperactivity disorder in adults using illicit psychostimulants: A systematic review. *Australian and New Zealand Journal of Psychiatry*, 51(9), 876–885.
- Cook, J. A. (2011). Associations between use of crack cocaine and HIV-1 disease progression: Research findings and implications for mother-to-infant transmission. *Life Sciences*, 88(21–22), 931–939.
- Cooper, B. E., & Sejnowski, C. A. (2013). Serotonin syndrome: Recognition and treatment. *AACN Advanced Critical Care*, 24(1), 15–20.
- Copersino, M. L., Schretlen, D. J., Fitzmaurice, G. M., Lukas, S. E., Faberman, J., Sokoloff, J., & Weiss, R. D. (2012). Effects of cognitive impairment on substance abuse treatment attendance: Predictive validation of a brief cognitive screening measure. *American Journal of Drug and Alcohol Abuse*, 38(3), 246–250.
- Corral-Verdugo, V., & Frias-Armenta, M. (2016). The sustainability of positive environments. *Environment, Development and Sustainability*, 18(4), 965–984.
- Corsi, K. F., Rinehart, D. J., Kwiatkowski, C. F., & Booth, R. E. (2010). Case management outcomes for women who use crack. *Journal of Evidence-Based Social Work*, 7(1), 30–40.

- Cortese, S., Panei, P., Arcieri, R., Germinario, E. A., Capuano, A., Margari, L., ... Curatolo, P. (2015). Safety of methylphenidate and atomoxetine in children with attention-deficit/hyperactivity disorder (ADHD): Data from the Italian National ADHD Registry. *CNS Drugs*, 29(10), 865–877.
- Cos, T. A., LaPollo, A. B., Aussendorf, M., Williams, J. M., Malayter, K., & Festinger, D. S. (2020). Do peer recovery specialists improve outcomes for individuals with substance use disorder in an integrative primary care setting? A program evaluation. *Journal of Clinical Psychology in Medical Settings*, 27(4), 704–715.
- Cosottile, D. W., & DeFulio, A. (2020). The compatibility of employment-based contingency management and vocational services at the Department of Veterans Affairs. *Psychology of Addictive Behaviors*, 34(1), 111–116.
- Courtney, K. E., & Ray, L. A. (2014). Methamphetamine: An update on epidemiology, pharmacology, clinical phenomenology, and treatment literature. *Drug and Alcohol Dependence*, 143, 11–21.
- Cousijn, J., Luijten, M., & Feldstein Ewing, S. W. (2018). Adolescent resilience to addiction: A social plasticity hypothesis. *Lancet Child and Adolescent Health*, 2(1), 69–78.
- Cox, K. B., Malte, C. A., & Saxon, A. J. (2017). Characteristics and service utilization of homeless veterans entering VA substance use treatment. *Psychological Services*, 14(2), 208–213.
- Craig, S. G., Davies, G., Schibuk, L., Weiss, M. D., & Hechtman, L. (2015). Long-term effects of stimulant treatment for ADHD: What can we tell our patients? *Current Developmental Disorders Reports*, 2(1), 1–9.
- Crane, C. A., Oberleitner, L. M. S., Devine, S., & Easton, C. J. (2014). Substance use disorders and intimate partner violence perpetration among male and female offenders. *Psychology of Violence*, 4(3), 322–333.
- Crawford, S., & Bath, N. (2013). Peer support models for people with a history of injecting drug use undertaking assessment and treatment for hepatitis C Virus infection. *Clinical Infectious Diseases*, 57(Suppl. 2), S75–S79.
- Cruikshank, C. C., & Dyer, K. R. (2009). A review of the clinical pharmacology of methamphetamine. *Addiction*, 104(7), 1085–1099.
- Cucciare, M. A., Ounpraseuth, S. T., Curran, G. M., & Booth, B. M. (2019). Predictors of substance use disorder and mental health treatment use among rural adults using stimulants over three years. *Substance Abuse*, 40(3), 363–370.
- Cumming, C., Kinner, S. A., McKetin, R., Li, I., & Preen, D. (2020). Methamphetamine use, health and criminal justice system outcomes: A systematic review. *Drug and Alcohol Review*, 39(5), 505–518.
- Cunha-Oliveira, T., Rego, A. C., Carvalho, F., & Oliveira, C. R. (2013). Medical toxicology of drugs of abuse. In P. M. Miller, S. A. Ball, M. E. Bates, A. W. Blume, K. M. Kampman, D. J. Kavanagh, M. E. Larimer, N. M. Petry, & P. De Witte (Eds.), *Comprehensive addictive behaviors and disorders: Vol. 1. Principles of addiction* (pp. 159–175). Academic Press.
- Cunha-Oliveira, T., Rego, A. C., & Oliveira, C. (2014). Cocaine as a neurotoxin. In R. Kostrzewa (Ed.), *Handbook of neurotoxicity* (pp. 277–297). Springer.
- Cunningham, C. O., Giovanniello, A., Kunins, H. V., Roose, R. J., Fox, A. D., & Sohler, N. L. (2013). Buprenorphine treatment outcomes among opioid-dependent cocaine users and non-users. *American Journal on Addictions*, 22(4), 352–357.
- Cunningham, E. B., Amin, J., Feld, J. J., Bruneau, J., Dalgard, O., Powis, J., ... Grebely, J. (2018). Adherence to sofosbuvir and velpatasvir among people with chronic HCV infection and recent injection drug use: The SIMPLIFY study. *International Journal of Drug Policy*, 62, 14–23.
- Dakwar, E., & Levin, F. R. (2013). Individual mindfulness-based psychotherapy for cannabis or cocaine dependence: A pilot feasibility trial. *American Journal on Addictions*, 22(6), 521–526.
- Dakwar, E., Nunes, E. V., Hart, C. L., Foltin, R. W., Mathew, S. J., Carpenter, K. M., ... Levin, F. R. (2019). A single ketamine infusion combined with mindfulness-based behavioral modification to treat cocaine dependence: A randomized clinical trial. *American Journal of Psychiatry*, 176(11), 923–930.
- Dallery, J., Raiff, B. R., Grabinski, M. J., & Marsch, L. A. (2019). Technology-based contingency management in the treatment of substance-use disorders. *Perspectives on Behavior Science*, 42(3), 445–464.
- Damon, W., McNeil, R., Milloy, M. J., Nosova, E., Kerr, T., & Hayashi, K. (2019). Residential eviction predicts initiation of or relapse into crystal methamphetamine use among people who inject drugs: A prospective cohort study. *Journal of Public Health*, 41(1), 36–45.
- Danielson, M. L., Bitsko, R. H., Ghandour, R. M., Holbrook, J. R., Kogan, M. D., & Blumberg, S. J. (2018). Prevalence of parent-reported ADHD diagnosis and associated treatment among U.S. children and adolescents, 2016. *Journal of Clinical Child and Adolescent Psychology*, 47(2), 199–212.
- Dasgupta, S., Tie, Y., Lemons-Lyn, A., Broz, D., Buchacz, K., & Shouse, R. L. (2020). HIV-positive persons who inject drugs experience poor health outcomes and unmet needs for care services. *AIDS Care*. Advance online publication. doi:10.1080/09540121.2020.1826396



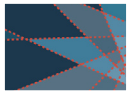
- da Silva Maia, A. F., Martins, F. T., da Silva Neto, L., Alves, R. B., & De Fátima, Â. (2017). Cocaethylene, the in vivo product of cocaine and ethanol, is a narcotic more potent than its precursors. *Acta Crystallographica Section C: Structural Chemistry*, 73(Pt. 10), 780–783.
- Davidow, J. Y., Foerde, K., Galván, A., & Shohamy, D. (2016). An upside to reward sensitivity: The hippocampus supports enhanced reinforcement learning in adolescence. *Neuron*, 92(1), 93–99.
- Daw, N. D., & Tobler, P. N. (2013). Value learning through reinforcement: The basis of dopamine and reinforcement learning. In P. W. Glimcher & E. Fehr (Eds.), *Neuroeconomics: Decision making and the brain* (2nd ed., pp. 283–298). Elsevier.
- De Crescenzo, F., Ciabattini, M., D'Alò, G. L., De Giorgi, R., Del Giovane, C., Cassar, C., ... Cipriani, A. (2018). Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: A systematic review and network meta-analysis. *PLoS Medicine*, 15(12), e1002715.
- De Giorgi, R., Cassar, C., Loreto D'Alò, G., Ciabattini, M., Minozzi, S., Economou, A., ... De Crescenzo, F. (2018). Psychosocial interventions in stimulant use disorders: A systematic review and qualitative synthesis of randomized controlled trials. *Rivista di Psichiatria*, 53(5), 233–255.
- Delaney, F. T., Stanley, E., & Bolster, F. (2020). The needle and the damage done: Musculoskeletal and vascular complications associated with injected drug use. *Insights into Imaging*, 11(1), 1–14.
- dela Peña, I., Gevorkiana, R., & Shi, W. X. (2015). Psychostimulants affect dopamine transmission through both dopamine transporter-dependent and independent mechanisms. *European Journal of Pharmacology*, 764, 562–570.
- Del Río, F. J., Cabello, F., & Fernández, I. (2015). Influence of substance use on the erectile response in a sample of drug users. *International Journal of Clinical and Health Psychology*, 15(1), 37–43.
- Deng, X., Huang, Z., Li, X., Li, Y., Wang, Y., Wu, D., ... Yang, X. (2012). Long-term follow-up of patients treated for psychotic symptoms that persist after stopping illicit drug use. *Shanghai Archives of Psychiatry*, 24(5), 271–278.
- Department of Health and Human Services. (2021, June 2). U.S. statistics. <https://www.hiv.gov/hiv-basics/overview/data-and-trends/statistics>
- Department of Housing and Urban Development. (2021). *The 2020 Annual Homeless Assessment Report (AHAR) to Congress: Pt. 1. Point-in-time estimates of homelessness*. <https://www.hudexchange.info/resource/6291/2020-ahar-part-1-pit-estimates-of-homelessness-in-the-us/>
- Des Jarlais, D. C. (2017). Harm reduction in the USA: The research perspective and an archive to David Purchase. *Harm Reduction Journal*, 14(1), 51.
- Des Jarlais, D. C., Feelemyer, J. P., Modi, S. N., Abdul-Quader, A., & Hagan, H. (2013). High coverage needle/syringe programs for people who inject drugs in low and middle income countries: A systematic review. *BMC Public Health*, 13, 53.
- De Sousa, A. (2013). Repetitive transcranial magnetic stimulation (rTMS) in the management of alcohol dependence and other substance abuse disorders: Emerging data and clinical relevance. *Basic and Clinical Neuroscience*, 4(3), 271–275.
- DeVito, E. E., Babuscio, T. A., Nich, C., Ball, S. A., & Carroll, K. M. (2014). Gender differences in clinical outcomes for cocaine dependence: Randomized clinical trials of behavioral therapy and disulfiram. *Drug and Alcohol Dependence*, 145, 156–167.
- Dezman, Z. D. W., Gorelick, D. A., Buchanan, L., & Soderstrom, C. A. (2020). 20-year mortality after discharge in a cohort of 1,099 former trauma inpatients with and without substance use disorders. *Injury*, 51(12), 2930–2937.
- Diaz, M., Tenney, C., Boyd, K. E., & Ford, J. A. (2021). Sexual identity and motivations for prescription drug misuse among U.S. adults. *LGBT Health*, 8(2), 107–115.
- Diaz, N., Horton, E. G., & Weiner, M. (2012). Dysthymia, major depression, and double depression among individuals receiving substance abuse treatment. *Health*, 4(12), 1229–1237.
- Dinger, J., Hinner, P., Reichert, J., & Rüdiger, M. (2017). Methamphetamine consumption during pregnancy—Effects on child health. *Pharmacopsychiatry*, 50(3), 107–113.
- Ditmore, M. H. (2013). *When sex work and drug use overlap: Considerations for advocacy and practice*. Harm Reduction International.
- Dodds, D., Koch, K., Buitrago-Mogollon, T., & Horstmann, S. (2019). Successful implementation of the eat sleep console model of care for infants with NAS in a community hospital. *Hospital Pediatrics*, 9(8), 632–638.
- Dos Santos, J. F., de Melo Bastos Cavalcante, C., Barbosa, F. T., Gitai, D., Duzzioni, M., Tilelli, C. Q., ... de Castro, O. W. (2018). Maternal, fetal and neonatal consequences associated with the use of crack cocaine during the gestational period: A systematic review and meta-analysis. *Archives of Gynecology and Obstetrics*, 298(3), 487–503.
- Dougherty, D. M., Olvera, R. L., Acheson, A., Hill-Kapturczak, N., Ryan, S. R., & Mathias, C. W. (2016). Acute effects of methylphenidate on impulsivity and attentional behavior among adolescents comorbid for ADHD and conduct disorder. *Journal of Adolescence*, 53, 222–230.
- Dougherty, M. M., & Marraffa, J. M. (2014). Phenothiazines. In P. Wexler (Ed.), *Encyclopedia of toxicology* (3rd ed., pp. 881–883). Academic Press.

- Drug Enforcement Administration. (2017). *Colombian cocaine production expansion contributes to rise in supply in the United States* (DEA-DCT-DIB-014-17).
- Drug Enforcement Administration. (2018). *Deadly contaminated cocaine widespread in Florida* (DEA-MIA-BUL-039-18).
- Drug Enforcement Administration. (2019). *2019 National Drug Threat Assessment* (DEA DCT DIR 007-20). U.S. Department of Justice.
- Drug Enforcement Administration. (2021). *2020 National Drug Threat Assessment* (DEA PRB 01-12-21-43). U.S. Department of Justice.
- Drug Enforcement Administration, Diversion Control Division. (n.d.). Controlled substance schedules. <https://www.deadiversion.usdoj.gov/schedules/>
- Drug Enforcement Administration, Diversion Control Division. (2019a). *Cocaine (street names: coke, snow, crack, rock)*. U.S. Department of Justice.
- Drug Enforcement Administration, Diversion Control Division. (2019b). *NFLIS-Drug Special Report: Methamphetamine reported in NFLIS, 2001–2017*. U.S. Department of Justice. Retrieved June 9, 2021, through <https://www.nflis.deadiversion.usdoj.gov/publicationsRedesign.xhtml>
- Ducci, F., & Goldman, D. (2012). The genetic basis of addictive disorders. *Psychiatric Clinics of North America*, 35(2), 495–519.
- Dufour, M., Nguyen, N., Bertrand, K., Perreault, M., Jutras-Aswad, D., Morvannou, A., ... Roy, É. (2016). Gambling problems among community cocaine users. *Journal of Gambling Studies*, 32(3), 1039–1053.
- Dumont, D. M., Allen, S. A., Brockmann, B. W., Alexander, N. E., & Rich, J. D. (2013). Incarceration, community health, and racial disparities. *Journal of Health Care for the Poor and Underserved*, 24(1), 78–88.
- Duncan, D. T., Goedel, W. C., Stults, C. B., Brady, W. J., Brooks, F. A., Blakely, J. S., & Hagen, D. (2018). A study of intimate partner violence, substance abuse, and sexual risk behaviors among gay, bisexual, and other men who have sex with men in a sample of geosocial-networking smartphone application users. *American Journal of Men's Health*, 12(2), 292–301.
- Dunn, A., & Gauthier, T. (2020). *An introductory guide for assessing and understanding common wounds with people who inject drugs*.
- Duong, J., Elia, C., Takayanagi, A., Lanzilotta, T., Ananda, A., & Miulli, D. (2018). The impact of methamphetamines in patients with traumatic brain injury, a retrospective review. *Clinical Neurology and Neurosurgery*, 170, 99–101.
- Eddie, D., Hoffman, L., Vilsaint, C., Abry, A., Bergman, B., Hoeppner, B., ... Kelly, J. F. (2019). Lived experience in new models of care for substance use disorder: A systematic review of peer recovery support services and recovery coaching. *Frontiers in Psychology*, 10, 1052.
- Edelman, E. J., Cole, C. A., Richardson, W., Boshnack, N., Jenkins, H., & Rosenthal, M. S. (2016). Stigma, substance use and sexual risk behaviors among HIV-infected men who have sex with men: A qualitative study. *Preventive Medicine Reports*, 3, 296–302.
- Ehlers, C. L., Gizer, I. R., Gilder, D. A., & Yehuda, R. (2013). Lifetime history of traumatic events in an American Indian community sample: Heritability and relation to substance dependence, affective disorder, conduct disorder and PTSD. *Journal of Psychiatric Research*, 47(2), 155–161.
- Eisinger, R. W., Dieffenbach, C. W., & Fauci, A. S. (2019). HIV viral load and transmissibility of HIV infection: Undetectable equals untransmittable. *JAMA*, 321(5), 451–452.
- Elkafrawi, D., Sisti, G., Araj, S., Khoury, A., Miller, J., & Rodriguez Echevarria, B. (2020). Risk factors for neonatal/maternal morbidity and mortality in African American women with placental abruption. *Medicina*, 56(4), 174.
- Elliott, R., Bohart, A. C., Watson, J. C., & Murphy, D. (2018). Therapist empathy and client outcome: An updated meta-analysis. *Psychotherapy (Chicago, Ill.)*, 55(4), 399–410.
- Ellis, C., Hoffman, W., Jaehnert, S., Plagge, J., Loftis, J. M., Schwartz, D., & Huckans, M. (2016). Everyday problems with executive dysfunction and impulsivity in adults recovering from methamphetamine addiction. *Addictive Disorders and Their Treatment*, 15(1), 1.
- Ellis, M. S., Kasper, Z. A., & Cicero, T. J. (2018). Twin epidemics: The surging rise of methamphetamine use in chronic opioid users. *Drug and Alcohol Dependence*, 193, 14–20.
- Eramah, M., Einstein, M., Mori, N., & Vakil, N. (2012). High mortality of cocaine-related ischemic colitis: A hybrid cohort/case-control study. *Gastrointestinal Endoscopy*, 75(6), 1226–1232.
- Ersche, K. D., Williams, G. B., Robbins, T. W., & Bullmore, E. T. (2013). Meta-analysis of structural brain abnormalities associated with stimulant drug dependence and neuroimaging of addiction vulnerability and resilience. *Current Opinion in Neurobiology*, 23(4), 615–624.
- Ethier, A. R., Kim, H. S., Hodgins, D. C., & McGrath, D. S. (2020). High rollers: Correlates of problematic cocaine use among a community sample of gamblers. *Journal of Gambling Studies*, 36(2), 513–525.
- Evans, M. K., Rosenbaum, L., Malina, D., Morrissey, S., & Rubin, E. J. (2020). Diagnosing and treating systemic racism. *New England Journal of Medicine*, 383(3), 274–276.



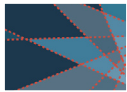
- Evans-Campbell, T., Walters, K. L., Pearson, C. R., & Campbell, C. D. (2012). Indian boarding school experience, substance use, and mental health among urban two-spirit American Indian/Alaska natives. *American Journal of Drug and Alcohol Abuse*, 38(5), 421–427.
- Fakhoury, M. (2014). The addicted human brain: An overview of imaging studies and their treatment implications. *Open Access Library Journal*, 1(7), 1–7.
- Fallin-Bennett, A., Elswick, A., & Ashford, K. (2020). Peer support specialists and perinatal opioid use disorder: Someone that's been there, lived it, seen it. *Addictive Behaviors*, 102, 106204.
- Famutimi, O., & Thompson, K. (2018). Trends in substance use treatment admissions among the homeless in the United States: 2005–2015. *Journal of Public Health Issues and Practices*, 2, 1–8.
- Farabee, D. (2018). Current and promising pharmacotherapies for substance use disorders among justice-involved populations. *European Journal on Criminal Policy and Research*, 24(2), 145–153.
- Farabee, D., Cousins, S. J., Brecht, M. L., Antonini, V. P., Lee, A. B., Brummer, J., ... Rawson, R. A. (2013). A comparison of four telephone-based counseling styles for recovering stimulant users. *Psychology of Addictive Behaviors*, 27(1), 223–229.
- Farabee, D., McCann, M., Brecht, M. L., Cousins, S. J., Antonini, V. P., Lee, A. B., ... Rawson, R. A. (2013). An analysis of relapse prevention factors and their ability to predict sustained abstinence following treatment completion. *American Journal on Addictions*, 22(3), 206–211.
- Farkas, J. (2021, April 5). *The Internet book of critical care. Sympathomimetic intoxication*. <https://emcrit.org/ibcc/symp/>
- Farooque, U., Okorie, N., Kataria, S., Shah, S. F., & Bollampally, V. C. (2020). Cocaine-induced headache: A review of pathogenesis, presentation, diagnosis, and management. *Cureus*, 12(8), e10128.
- Farrell, M., Martin, N. K., Stockings, E., Bórquez, A., Cepeda, J. A., Degenhardt, L., ... McKetin, R. (2019). Responding to global stimulant use: Challenges and opportunities. *Lancet*, 394(10209), 1652–1667.
- Farren, C. K., Hill, K. P., & Weiss, R. D. (2012). Bipolar disorder and alcohol use disorder: A review. *Current Psychiatry Reports*, 14(6), 659–666.
- Farronato, N. S., Dürsteler-Macfarland, K. M., Wiesbeck, G. A., & Petitjean, S. A. (2013). A systematic review comparing cognitive-behavioral therapy and contingency management for cocaine dependence. *Journal of Addictive Diseases*, 32(3), 274–287.
- Federal Bureau of Prisons. (2021, June 5). Offenses. Retrieved June 10, 2021, from https://www.bop.gov/about/statistics/statistics_inmate_offenses.jsp
- Ferrucci, M., Limanaqi, F., Ryskalin, L., Biagioni, F., Busceti, C. L., & Fornai, F. (2019). The effects of amphetamine and methamphetamine on the release of norepinephrine, dopamine and acetylcholine from the brainstem reticular formation. *Frontiers in Neuroanatomy*, 13, 48.
- Flanagan, J. C., Korte, K. J., Killeen, T. K., & Back, S. E. (2016). Concurrent treatment of substance use and PTSD. *Current Psychiatry Reports*, 18(8), 70.
- Fleming, T., Barker, A., Ivins, A., Vakharia, S., & McNeil, R. (2020). Stimulant safe supply: A potential opportunity to respond to the overdose epidemic. *Harm Reduction Journal*, 17(1), 1–6.
- Flentje, A., Heck, N. C., & Sorensen, J. L. (2014). Characteristics of transgender individuals entering substance abuse treatment. *Addictive Behaviors*, 39(5), 969–975.
- Fletcher, J. B., Shoptaw, S., Peck, J. A., & Reback, C. J. (2014). Contingency management reduces symptoms of psychological and emotional distress among homeless, substance-dependent men who have sex with men. *Mental Health and Substance Use*, 7(4), 420–430.
- Fletcher, J. B., Swendeman, D., & Reback, C. J. (2018). Mental health and substance use disorder comorbidity among methamphetamine-using men who have sex with men. *Journal of Psychoactive Drugs*, 50(3), 206–213.
- Fluyau, D., Mitra, P., & Lortie, K. (2019). Antipsychotics for amphetamine psychosis: A systematic review. *Frontiers in Psychiatry*, 10, 740.
- Foltin, R. W., Haney, M., Bedi, G., & Evans, S. M. (2016). Modafinil decreases cocaine choice in human cocaine smokers only when the response requirement and the alternative reinforcer magnitude are large. *Pharmacology, Biochemistry, and Behavior*, 150–151, 8–13.
- Foltin, R. W., Haney, M., Rubin, E., Reed, S. C., Vadhan, N., Balter, R., & Evans, S. M. (2015). Development of translational preclinical models in substance abuse: Effects of cocaine administration on cocaine choice in humans and non-human primates. *Pharmacology, Biochemistry, and Behavior*, 134, 12–21.
- Fong, C., Matusow, H., Cleland, C. M., & Rosenblum, A. (2015). Characteristics of non-opioid substance misusers among patients enrolling in opioid treatment programs: A latent class analysis. *Journal of Addictive Diseases*, 34(2–3), 141–150.
- Food and Drug Administration. (2017, September 14). FDA permits marketing of mobile medical application for substance use disorder [Press release]. <https://www.fda.gov/news-events/press-announcements/fda-permits-marketing-mobile-medical-application-substance-use-disorder>

- Food and Drug Administration. (2019, October 3). *FDA approves second drug to prevent HIV infection as part of ongoing efforts to end the HIV epidemic* [Press release]. <https://www.fda.gov/news-events/press-announcements/fda-approves-second-drug-prevent-hiv-infection-part-ongoing-efforts-end-hiv-epidemic>
- Forray, A., & Foster, D. (2015). Substance use in the perinatal period. *Current Psychiatry Reports*, 17(11), 91.
- Foster, M. A., Hofmeister, M. G., Kupronis, B. A., Lin, Y., Xia, G.-L., Yin, S., & Teshale, E. (2019). Increase in hepatitis A virus infections – United States, 2013–2018. *Morbidity and Mortality Weekly Report*, 68(18), 413–415.
- Foulds, J. A., Boden, J. M., McKetin, R., & Newton-Howes, G. (2020). Methamphetamine use and violence: Findings from a longitudinal birth cohort. *Drug and Alcohol Dependence*, 207, 107826.
- Fratto, G., & Manzon, L. (2014). Use of psychotropic drugs and associated dental diseases. *International Journal of Psychiatry in Medicine*, 48(3), 185–197.
- Frazer, Z., McConnell, K., & Jansson, L. M. (2019). Treatment for substance use disorders in pregnant women: Motivators and barriers. *Drug and Alcohol Dependence*, 205, 107652.
- Freeborn, K., & Portillo, C. J. (2018). Does pre-exposure prophylaxis for HIV prevention in men who have sex with men change risk behaviour? A systematic review. *Journal of Clinical Nursing*, 27(17–18), 3254–3265.
- Friedman, S. M., Margo, C. E., Konicki, M., Campanelli, M., Jampol, L. M., & Plous, O. Z. (2010). Bilateral vascular occlusions of the anterior visual pathway and cocaine abuse. *Retinal Cases and Brief Reports*, 4(2), 95–98.
- Friesen, B. J., Cross, T. L., Jivanjee, P., Thirstrup, A., Bandurraga, A., Gowen, L. K., & Rountree, J. (2015). Meeting the transition needs of urban American Indian/Alaska Native youth through culturally based services. *Journal of Behavioral Health Services and Research*, 42(2), 191–205.
- Galloway, G. P., Singleton, E. G., Buscemi, R., Baggott, M. J., Dickerhoof, R. M., & Mendelson, J. E. (2010). An examination of drug craving over time in abstinent methamphetamine users. *American Journal on Addictions*, 19(6), 510–514.
- Garg, L., Akbar, G., Agrawal, S., Agarwal, M., Khaddour, L., Handa, R., ... Dalal, B. D. (2017). Drug-induced pulmonary arterial hypertension: A review. *Heart Failure Reviews*, 22(3), 289–297.
- Garofalo, R., Hotton, A. L., Kuhns, L. M., Gratz, B., & Mustanski, B. (2016). Incidence of HIV infection and sexually transmitted infections and related risk factors among very young men who have sex with men. *Journal of Acquired Immune Deficiency Syndromes*, 72(1), 79–86.
- Gastfriend, D. R. (2018, March 14). *Contingency management: The greatest unused treatment in opioid use disorder* [Webinar handout]. Florida Alcohol and Drug Abuse Association.
- Geisner, I. M., Huh, D., Crouse, J. M., Lostutter, T. W., Kilmer, J., & Larimer, M. E. (2016). Exploring the relationship between stimulant use and gambling in college students. *Journal of Gambling Studies*, 32(3), 1001–1016.
- Genberg, B. L., Astemborski, J., Vlahov, D., Kirk, G. D., & Mehta, S. H. (2015). Incarceration and injection drug use in Baltimore, Maryland. *Addiction*, 110(7), 1152–1159.
- George, T. C., Freet, D. J., Cross, J. M., & Huzar, T. F. (2019). Levamisole-induced vasculitis. *Journal of the American Academy of Physician Assistants*, 32(1), 23–27.
- Gerstein, D. R., Johnson, R. A., Harwood, H. J., Fountain, D., Suter, N., & Malloy, K. (Eds.). (1994). *Evaluating recovery services: The California Drug and Alcohol Treatment Assessment (CALDATA)*. California Department of Alcohol and Drug Programs, Resource Center.
- Gibson, B. A., Ghosh, D., Morano, J. P., & Altice, F. L. (2014). Accessibility and utilization patterns of a mobile medical clinic among vulnerable populations. *Health and Place*, 28, 153–166.
- Giorgetti, R., Tagliabracci, A., Schifano, F., Zaami, S., Marinelli, E., & Busardò, F. P. (2017). When “chems” meet sex: A rising phenomenon called “chemsex.” *Current Neuropharmacology*, 15(5), 762–770.
- Giovazolias, T., & Themeli, O. (2014). Social learning conceptualization for substance abuse: Implications for therapeutic interventions. *European Journal of Counselling Psychology*, 3(1), 69–88.
- Gizzi, M. C., & Gerkin, P. (2010). Methamphetamine use and criminal behavior. *International Journal of Offender Therapy and Comparative Criminology*, 54(6), 915–936.
- Glasner-Edwards, S., & Mooney, L. J. (2014). Methamphetamine psychosis: Epidemiology and management. *CNS Drugs*, 28(12), 1115–1126.
- Glasner-Edwards, S., Mooney, L. J., Ang, A., Garneau, H. C., Hartwell, E., Brecht, M. L., & Rawson, R. A. (2017). Mindfulness-Based Relapse Prevention for stimulant dependent adults: A pilot randomized clinical trial. *Mindfulness*, 8(1), 126–135.
- Glasner-Edwards, S., Mooney, L. J., Ang, A., Hillhouse, M., & Rawson, R. (2013). Does posttraumatic stress disorder (PTSD) affect post-treatment methamphetamine use? *Journal of Dual Diagnosis*, 9(2), 123–128.



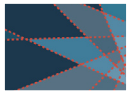
- Glass, J. E., Nunes, E. V., & Bradley, K. A. (2020, March 11). Contingency management: A highly effective treatment for substance use disorders and the legal barriers that stand in its way. *Health Affairs Blog*. <https://www.healthaffairs.org/doi/10.1377/hblog20200305.965186/full/>
- Glynn, T. R., & van den Berg, J. J. (2017). A systematic review of interventions to reduce problematic substance use among transgender individuals: A call to action. *Transgender Health*, 2(1), 45–59.
- Godinet, M. T., McGlinn, L., Nelson, D., & Vakalahi, H. O. (2020). Factors contributing to substance misuse treatment completion among Native Hawaiians, Other Pacific Islanders, and Asian Americans. *Substance Use and Misuse*, 55(1), 133–146.
- Goel, N., Pullman, J. M., & Coco, M. (2014). Cocaine and kidney injury: A kaleidoscope of pathology. *Clinical Kidney Journal*, 7(6), 513–517.
- Goldstein, R. B., Smith, S. M., Chou, S. P., Saha, T. D., Jung, J., Zhang, H., ... Grant, B. F. (2016). The epidemiology of DSM-5 posttraumatic stress disorder in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions–III. *Social Psychiatry and Psychiatric Epidemiology*, 51(8), 1137–1148.
- González-Baeza, A., Dolengevich-Segal, H., Pérez-Valero, I., Cabello, A., Téllez, M. J., Sanz, J., ... Ryan, P. (2018). Sexualized drug use (chemsex) is associated with high-risk sexual behaviors and sexually transmitted infections in HIV-positive men who have sex with men: Data from the U-SEX GESIDA 9416 study. *AIDS Patient Care and STDs*, 32(3), 112–118.
- Gouin, K., Murphy, K., Shah, P. S., & Knowledge Synthesis Group on Determinants of Low Birth Weight and Preterm Births. (2011). Effects of cocaine use during pregnancy on low birthweight and preterm birth: Systematic review and meta-analyses. *American Journal of Obstetrics and Gynecology*, 204(4), 340.e1–340.e12.
- Gould, T. J. (2010). Addiction and cognition. *Addiction Science and Clinical Practice*, 5(2), 4–14.
- Government Accountability Office. (n.d.). Tribal and Native American issues. <https://www.gao.gov/tribal-and-native-american-issues>
- Gowin, J. L., Ernst, M., Ball, T., May, A. C., Sloan, M. E., Tapert, S. F., & Paulus, M. P. (2019). Using neuroimaging to predict relapse in stimulant dependence: A comparison of linear and machine learning models. *NeuroImage: Clinical*, 21, 101676.
- Granado, N., Ares-Santos, S., & Moratalla, R. (2013). Methamphetamine and Parkinson's disease. *Parkinson's Disease*, 2013, 308052.
- Grant, B. F., Chou, S. P., Saha, T. D., Pickering, R. P., Kerridge, B. T., Ruan, W. J., ... Hasin, D. S. (2017). Prevalence of 12-month alcohol use, high-risk drinking, and DSM-IV alcohol use disorder in the United States, 2001–2002 to 2012–2013: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *JAMA Psychiatry*, 74(9), 911–923.
- Grant, B. F., Goldstein, R. B., Saha, T. D., Chou, S. P., Jung, J., Zhang, H., ... Hasin, D. S. (2015). Epidemiology of DSM-5 alcohol use disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions–III. *JAMA Psychiatry*, 72(8), 757–766.
- Grant, B. F., Saha, T. D., Ruan, W. J., Goldstein, R. B., Chou, S. P., Jung, J., ... Hasin, D. S. (2016). Epidemiology of DSM-5 drug use disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions–III. *JAMA Psychiatry*, 73(1), 39–47.
- Grant, J. M., Mottet, L. A., Tanis, J., Harrison, J., Herman, J. L., & Keisling, M. (2011). *Injustice at every turn: A report of the National Transgender Discrimination Survey*. National Center for Transgender Equality and National Gay and Lesbian Task Force.
- Grant, S., Colaiaco, B., Motala, A., Shanman, R., Booth, M., Sorbero, M., & Hempel, S. (2017). Mindfulness-Based Relapse Prevention for substance use disorders: A systematic review and meta-analysis. *Journal of Addiction Medicine*, 11(5), 386–396.
- Greydanus, D. E. (2006). Stimulant misuse: Strategies to manage a growing problem. In *Use and misuse of stimulants: A guide for school health professionals* (pp. 17–23). American College Health Association.
- Griffin, D., & Cha, S. (2019). Cocaine: A provoking risk factor in venous thromboembolism. *Cureus*, 11(12), e6520.
- Grigg, J., Manning, V., Arunogiri, S., Volpe, I., Frei, M., Phan, V., ... Lubman D. I. (2018). *Methamphetamine treatment guidelines: Practice guidelines for health professionals* (2nd ed.). Turning Point.
- Grund, J.-P., Coffin, P., & Jauffret-Roustide, M., Dijkstra, M., Bruin, D., & Blanken, P. (2010). The fast and furious: Cocaine, amphetamines and harm reduction. In T. Rhodes & D. Hedrich (Eds.), *Harm reduction: Evidence, impact and challenges* (pp. 205–254). Publications Office of the European Union.
- Guck, D., & Munyon, R. (2018). Bilateral spontaneous pneumothoraces with spontaneous pneumomediastinum: An intravenous methamphetamine complication. *Respiratory Medicine Case Reports*, 25, 4–5.
- Guina, J., & Merrill, B. (2018). Benzodiazepines I: Upping the care on downers—The evidence of risks, benefits, and alternatives. *Journal of Clinical Medicine*, 7(2), 17.

- Hadland, S. E., Yule, A. M., Levy, S. J., Hallett, E., Silverstein, M., & Bagley, S. M. (2021). Evidence-based treatment of young adults with substance use disorders. *Pediatrics*, 147(Suppl. 2), S204–S214.
- Hall, M. G., Alhassoon, O. M., Stern, M. J., Wollman, S. C., Kimmel, C. L., Perez-Figueroa, A., & Radua, J. (2015). Gray matter abnormalities in cocaine versus methamphetamine-dependent patients: A neuroimaging meta-analysis. *American Journal of Drug and Alcohol Abuse*, 41(4), 290–299.
- Hall, M. G., Hauson, A. O., Wollman, S. C., Allen, K. E., Connors, E. J., Stern, M. J., ... Grant, I. (2018). Neuropsychological comparisons of cocaine versus methamphetamine users: A research synthesis and meta-analysis. *American Journal of Drug and Alcohol Abuse*, 44(3), 277–293.
- Halpin, L. E., Collins, S. A., & Yamamoto, B. K. (2014). Neurotoxicity of methamphetamine and 3,4-methylenedioxymethamphetamine. *Life Sciences*, 97(1), 37–44.
- Hammoud, M. A., Vaccher, S., Jin, F., Bourne, A., Haire, B., Maher, L., ... Prestage, G. (2018). The new MTV generation: Using methamphetamine, Truvada™, and Viagra™ to enhance sex and stay safe. *International Journal of Drug Policy*, 55, 197–204.
- Han, Y., Lin, V., Wu, F., & Hser, Y.-I. (2016). Gender comparisons among Asian American and Pacific Islander patients in drug dependency treatment. *Substance Use and Misuse*, 51(6), 752–762.
- Han, Y., Yan, W., Zheng, Y., Khan, M. Z., Yuan, K., & Lu, L. (2019). The rising crisis of illicit fentanyl use, overdose, and potential therapeutic strategies. *Translational Psychiatry*, 9(1), 1–9.
- Hanieh, E., Musa, A.-R., & Jureidini, J. (2013). *The AGRO+ model*.
- Harada, T., Tsutomi, H., Mori, R., & Wilson, D. B. (2018). Cognitive-behavioural treatment for amphetamine-type stimulants (ATS)-use disorders. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.CD011315.pub2
- Hargraves, D., White, C., Frederick, R., Cinibulk, M., Peters, M., Young, A., & Elder, N. (2017). Implementing SBIRT (Screening, Brief Intervention and Referral to Treatment) in primary care: Lessons learned from a multi-practice evaluation portfolio. *Public Health Reviews*, 38, 31.
- Hariri, L., & Patel, J. (2021). Vasodilators. In *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK554423/>
- Harris, A. M., Iqbal, K., Schillie, S., Britton, J., Kainer, M. A., Tressler, S., & Vellozzi, C. (2016). Increases in acute hepatitis B virus infections – Kentucky, Tennessee, and West Virginia, 2006–2013. *Morbidity and Mortality Weekly Report*, 65(3), 47–50.
- Harrison, J., Grant, J., & Herman, J. L. (2012). A gender not listed here: Genderqueers, gender rebels and otherwise in the National Transgender Discrimination Study. *LGBT Policy Journal at the Harvard Kennedy School*, 2, 13–24.
- Harro, J. (2015). Neuropsychiatric adverse effects of amphetamine and methamphetamine. *International Review of Neurobiology*, 120, 179–204.
- Hart, C. L., Csete, J., & Habibi, D. (2014). *Methamphetamine: Fact vs. fiction and lessons from the crack hysteria*. https://www.opensocietyfoundations.org/publications/methamphetamine-dangers-exaggerated#publications_download
- Hart, C. L., Marvin, C. B., Silver, R., & Smith, E. E. (2012). Is cognitive functioning impaired in methamphetamine users? A critical review. *Neuropsychopharmacology*, 37(3), 586–608.
- Hartnett, K. P., Jackson, K. A., Felsen, C., McDonald, R., Bardossy, A. C., Gokhale, R. H., ... Dumyati, G. (2019). Bacterial and fungal infections in persons who inject drugs—Western New York, 2017. *Morbidity and Mortality Weekly Report*, 68(26), 583–586.
- Hartwell, E. E., Moallem, N. R., Courtney, K. E., Glasner-Edwards, S., & Ray, L. A. (2016). Sex differences in the association between internalizing symptoms and craving in methamphetamine users. *Journal of Addiction Medicine*, 10(6), 395–401.
- Hartwell, K., & Brady, K. (2018). Determining appropriate levels of care for treatment of substance use disorders. *UpToDate*. Retrieved March 19, 2021, from <https://www.uptodate.com/contents/determining-appropriate-levels-of-care-for-treatment-of-substance-use-disorders>
- Hartzler, B., & Garrett, S. (2016). Interest and preferences for contingency management design among addiction treatment clientele. *American Journal of Drug and Alcohol Abuse*, 42(3), 287–295.
- Hasin, D. S., & Grant, B. F. (2015). The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Waves 1 and 2: Review and summary of findings. *Social Psychiatry and Psychiatric Epidemiology*, 50(11), 1609–1640.
- Hasin, D., & Kilcoyne, B. (2012). Comorbidity of psychiatric and substance use disorders in the United States: Current issues and findings from the NESARC. *Current Opinion in Psychiatry*, 25(3), 165–171.
- Hasin, D. S., Sarvet, A. L., Meyers, J. L., Saha, T. D., Ruan, W. J., Stohl, M., & Grant, B. F. (2018). Epidemiology of Adult DSM-5 major depressive disorder and its specifiers in the United States. *JAMA Psychiatry*, 75(4), 336–346.
- Havakuk, O., Rezkalla, S. H., & Kloner, R. A. (2017). The cardiovascular effects of cocaine. *Journal of the American College of Cardiology*, 70(1), 101–113.



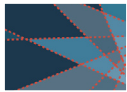
- Hawk, K., & D'Onofrio, G. (2018). Emergency department screening and interventions for substance use disorders. *Addiction Science and Clinical Practice*, 13(1), 1–6.
- Hayley, A. C., Downey, L. A., Shiferaw, B., & Stough, C. (2016). Amphetamine-type stimulant use and the risk of injury or death as a result of a road-traffic accident: A systematic review of observational studies. *European Neuropsychopharmacology*, 26(6), 901–922.
- Heal, D. J., Smith, S. L., Gosden, J., & Nutt, D. J. (2013). Amphetamine, past and present: A pharmacological and clinical perspective. *Journal of Psychopharmacology*, 27(6), 479–496.
- Healthy People 2030. (n.d.). Social determinants of health. U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. <https://health.gov/healthypeople/objectives-and-data/social-determinants-health>
- Hedegaard, H., Bastian, B. A., Trinidad, J. P., Spencer, M., & Warner, M. (2018). Drugs most frequently involved in drug overdose deaths: United States, 2011–2016. *National Vital Statistics Reports*, 67(9), 1–14.
- Hedges, D. M., O'Bray, J. D., Yorgason, J. T., Jang, E. Y., Weerasekara, V. K., Uys, J. D., Bellinger, F. P., & Steffensen, S. C. (2018). Methamphetamine induces dopamine release in the nucleus accumbens through a sigma receptor-mediated pathway. *Neuropsychopharmacology*, 43(6), 1405–1414.
- Hellem, T., Shi, X., Latendresse, G., & Renshaw, P. F. (2015). The utility of magnetic resonance spectroscopy for understanding substance use disorders: A systematic review of the literature. *Journal of the American Psychiatric Nurses Association*, 21(4), 244–275.
- Hellem, T. L., Lundberg, K. J., & Renshaw, P. F. (2015). A review of treatment options for co-occurring methamphetamine use disorders and depression. *Journal of Addictions Nursing*, 26(1), 14–23; quiz E1.
- Hendershot, C. S., Witkiewitz, K., George, W. H., & Marlatt, G. A. (2011). Relapse prevention for addictive behaviors. *Substance Abuse Treatment, Prevention, and Policy*, 6, 17.
- Henning, A., Kurtom, M., & Espiridion, E. D. (2019). A case study of acute stimulant-induced psychosis. *Cureus*, 11(2), e4126.
- Hennissen, L., Bakker, M. J., Banaschewski, T., Carucci, S., Coghill, D., Danckaerts, M., ... Buitelaar, J. K. (2017). Cardiovascular effects of stimulant and non-stimulant medication for children and adolescents with ADHD: A systematic review and meta-analysis of trials of methylphenidate, amphetamines and atomoxetine. *CNS Drugs*, 31(3), 199–215.
- Herbeck, D. M., Brecht, M. L., Christou, D., & Lovinger, K. (2014). A qualitative study of methamphetamine users' perspectives on barriers and facilitators of drug abstinence. *Journal of Psychoactive Drugs*, 46(3), 215–225.
- Hetea, A., Cosconel, C., Stanescu, A. A. M., & Simionescu, A. A. (2019). Alcohol and psychoactive drugs in pregnancy. *Maedica*, 14(4), 397–401.
- Hibbert, M. P., Porcellato, L. A., Brett, C. E., & Hope, V. D. (2019). Associations with drug use and sexualised drug use among women who have sex with women (WSW) in the UK: Findings from the LGBT Sex and Lifestyles Survey. *International Journal of Drug Policy*, 74, 292–298.
- Hirshfield, S., Schrimshaw, E. W., Stall, R. D., Margolis, A. D., Downing, Jr., M. J., & Chiasson, M. A. (2015). Drug use, sexual risk, and syndemic production among men who have sex with men who engage in group sexual encounters. *American Journal of Public Health*, 105(9), 1849–1858.
- Hodgkins, P., Shaw, M., Coghill, D., & Hechtman, L. (2012). Amphetamine and methylphenidate medications for attention-deficit/hyperactivity disorder: Complementary treatment options. *European Child and Adolescent Psychiatry*, 21(9), 477–492.
- Hoffman, R. S. (2010). Treatment of patients with cocaine-induced arrhythmias: Bringing the bench to the bedside. *British Journal of Clinical Pharmacology*, 69(5), 448–457.
- Hoffman, W. F., Jacobs, M. B., Dennis, L. E., McCready, H. D., Hickok, A. W., Smith, S. B., & Kohno, M. (2020). Psychopathy and corticostriatal connectivity: The link to criminal behavior in methamphetamine dependence. *Frontiers in Psychiatry*, 11, 90.
- Holmskov, M., Storebø, O. J., Moreira-Maia, C. R., Ramstad, E., Magnusson, F. L., Krogh, H. B., ... Simonsen, E. (2017). Gastrointestinal adverse events during methylphenidate treatment of children and adolescents with attention deficit hyperactivity disorder: A systematic review with meta-analysis and Trial Sequential Analysis of randomised clinical trials. *PLoS One*, 12(6), e0178187.
- Holmwood, C., & Gowing, L. (2019). *Acute presentations related to methamphetamine use clinical guideline for adults* (Version No. 2.0, Clinical Guideline No.: CG284). Government of South Australia, SA Health.
- Holt, L. J., Schepis, T. S., Looby, A., Marsh, E., Marut, P., & Feinn, R. (2020). How to say “no” most effectively: Evaluating resistance strategies for prescription stimulant diversion to inform preventive interventions. *Journal of American College Health*, 68(8), 872–882.
- Hser, Y.-I., Evans, E., Huang, D., Weiss, R., Saxon, A., Carroll, K. M., ... Ling, W. (2016). Long-term outcomes after randomization to buprenorphine/naloxone versus methadone in a multi-site trial. *Addiction*, 111(4), 695–705.

- Hser, Y.-I., & Mooney, L. J. (2021). Integrating telemedicine for medication treatment for opioid use disorder in rural primary care: Beyond the COVID pandemic. *Journal of Rural Health*, 37(1), 246–248.
- Hulsebos, I. F., Pham, C. H., Collier, Z. J., Fang, M., Vrouwe, S. Q., Sugiyama, A., ... Gillenwater, J. (2020). Stimulant abuse in burn patients is associated with an increased use of hospital resources. *Journal of Burn Care and Research*, 41(5), 921–925.
- Human Rights Campaign. (n.d.). Transgender and non-binary people FAQ. <https://www.hrc.org/resources/transgender-and-non-binary-faq>
- Hunt, D., Kuck, S., & Truitt, L. (2006). *Methamphetamine use: Lessons learned*. Abt Associates.
- Hunt, G. E., Siegfried, N., Morley, K., Sitharthan, T., & Cleary, M. (2019). Psychosocial interventions for people with both severe mental illness and substance misuse. *Schizophrenia Bulletin*, 40(1), 18–20.
- Huybrechts, K. F., Bröms, G., Christensen, L. B., Einarsdóttir, K., Engeland, A., Furu, K., ... Bateman, B. T. (2018). Association between methylphenidate and amphetamine use in pregnancy and risk of congenital malformations: A cohort study from the International Pregnancy Safety Study Consortium. *JAMA Psychiatry*, 75(2), 167–175.
- Indave, B. I., Sordo, L., Bravo, M. J., Sarasa-Renedo, A., Fernández-Balbuena, S., De la Fuente, L., ... Barrio, G. (2018). Risk of stroke in prescription and other amphetamine-type stimulants use: A systematic review. *Drug and Alcohol Review*, 37(1), 56–69.
- Indian Health Service. (n.d.). Two-Spirit. <https://www.ihs.gov/lgbt/health/twospirit/>
- Iqbal, K., Kleven, R. M., Kainer, M. A., Baumgartner, J., Gerard, K., Poissant, T., ... Teshale, E. (2015). Epidemiology of acute hepatitis B in the United States from population-based surveillance, 2006–2011. *Clinical Infectious Diseases*, 61(4), 584–592.
- Jackson, K. A., Bohm, M. K., Brooks, J. T., Asher, A., Nadle, J., Bamberg, W. M., ... See, I. (2018). Invasive methicillin-resistant *Staphylococcus aureus* infections among persons who inject drugs—Six sites, 2005–2016. *Morbidity and Mortality Weekly Report*, 67(22), 625–628.
- Jaffe, A., Molnar, S., Williams, N., Wong, E., Todd, T., Caputo, C., ... Ye, S. (2016). Review and recommendations for drug testing in substance use treatment contexts. *Journal of Reward Deficiency Syndrome and Addiction Science*, 2(1), 28–45.
- Jan, R. K., Kydd, R. R., & Russell, B. R. (2012). Functional and structural brain changes associated with methamphetamine abuse. *Brain Sciences*, 2(4), 434–482.
- Javanbakht, M., Ragsdale, A., Shoptaw, S., & Gorbach, P. M. (2019). Transactional sex among men who have sex with men: Differences by substance use and HIV status. *Journal of Urban Health*, 96(3), 429–441.
- Jeal, N., Macleod, J., Turner, K., & Salisbury, C. (2015). Systematic review of interventions to reduce illicit drug use in female drug-dependent street sex workers. *BMJ Open*, 5(11), e009238.
- Ji, Y., Kujtan, L., & Kershner, D. (2012). Acute endocarditis in intravenous drug users: A case report and literature review. *Journal of Community Hospital Internal Medicine Perspectives*, 2(1).
- Jiménez-Correa, U., Santana-Miranda, R., Barrera-Medina, A., Martínez-Núñez, J. M., Marín-Agudelo, H. A., Poblano, A., ... Hernández-Berber, I. (2020). Parasomnias in patients with addictions—A systematic review. *CNS Spectrums*, 1–8.
- Johns Hopkins Medicine. (n.d.-a). Status epilepticus. <https://www.hopkinsmedicine.org/health/conditions-and-diseases/status-epilepticus>
- Johns Hopkins Medicine. (n.d.-b). Thrombotic microangiopathy. https://www.hopkinsmedicine.org/nephrology/tm_sperati
- Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Patrick, M. E. (2020). *Monitoring the Future National Survey Results on Drug Use 1975–2019: Overview, key findings on adolescent drug use*. University of Michigan, Institute for Social Research.
- Jones, A. W. (2019). Forensic drug profile: Cocaethylene. *Journal of Analytical Toxicology*, 43(3), 155–160.
- Jones, C. M., Compton, W. M., & Mustaquim, D. (2020). Patterns and characteristics of methamphetamine use among adults—United States, 2015–2018. *Morbidity and Mortality Weekly Report*, 69(12), 317–323.
- Jones, P., Mutsunguma, R., & Prahlow, J. A. (2014). Accidental death via intravaginal absorption of methamphetamine. *Forensic Science, Medicine, and Pathology*, 10(2), 234–238.
- Jordan, A., Babuscio, T., Nich, C., & Carroll, K. M. (2021). A feasibility study providing substance use treatment in the Black church. *Journal of Substance Abuse Treatment*, 124, 108218.
- Jordan, A. E., Perlman, D. C., Neurer, J., Smith, D. J., Des Jarlais, D. C., & Hagan, H. (2017). Prevalence of hepatitis C virus infection among HIV+ men who have sex with men: A systematic review and meta-analysis. *International Journal of STD and AIDS*, 28(2), 145–159.
- Kadri, A. N., Wilner, B., Hernandez, A. V., Nakhoul, G., Chahine, J., Griffin, B., ... Harb, S. C. (2019). Geographic trends, patient characteristics, and outcomes of infective endocarditis associated with drug abuse in the United States from 2002 to 2016. *Journal of the American Heart Association*, 8(19), e012969.
- Kalvar, A., & Medaglia, J. D. (2018). Evidence of brain modularity. In T. K. Shackelford & V. A. Weekes-Shackelford (Eds.), *Encyclopedia of evolutionary psychological science*. Springer International Publishing.



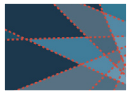
- Kampman, K. M. (2019). The treatment of cocaine use disorder. *Science Advances*, 5(10), eaax1532.
- Kampman, K., & Jarvis, M. (2015). American Society of Addiction Medicine (ASAM) national practice guideline for the use of medications in the treatment of addiction involving opioid use. *Journal of Addiction Medicine*, 9(5), 358–367.
- Kaplan, G. B., Heinrichs, S. C., & Carey, R. J. (2011). Treatment of addiction and anxiety using extinction approaches: Neural mechanisms and their treatment implications. *Pharmacology, Biochemistry, and Behavior*, 97(3), 619–625.
- Kariisa, M., Scholl, L., Wilson, N., Seth, P., & Hoots, B. (2019). Drug overdose deaths involving cocaine and psychostimulants with abuse potential—United States, 2003–2017. *Morbidity and Mortality Weekly Report*, 68(17), 388–395.
- Karila, L., Weinstein, A., Aubin, H. J., Benyamina, A., Reynaud, M., & Batki, S. L. (2010). Pharmacological approaches to methamphetamine dependence: A focused review. *British Journal of Clinical Pharmacology*, 69(6), 578–592.
- Katzman, M. A., Bilkey, T. S., Chokka, P. R., Fallu, A., & Klassen, L. J. (2017). Adult ADHD and comorbid disorders: Clinical implications of a dimensional approach. *BMC Psychiatry*, 17(1), 302.
- Kaye, S., Darke, S., & Torok, M. (2013). Attention deficit hyperactivity disorder (ADHD) among illicit psychostimulant users: A hidden disorder? *Addiction*, 108(5), 923–931.
- Keane, T. M., Rubin, A., Lachowicz, M., Brief, D., Enggasser, J. L., Roy, M., ... Rosenbloom, D. (2014). Temporal stability of DSM-5 posttraumatic stress disorder criteria in a problem-drinking sample. *Psychological Assessment*, 26(4), 1138–1145.
- Kecojevic, A., Corliss, H. L., & Lankenau, S. E. (2015). Motivations for prescription drug misuse among young men who have sex with men (YMSM) in Philadelphia. *International Journal of Drug Policy*, 26(8), 764–771.
- Kecojevic, A., Jun, H.-J., Reisner, S. L., & Corliss, H. L. (2017). Concurrent polysubstance use in a longitudinal study of US youth: Associations with sexual orientation. *Addiction*, 112(4), 614–624.
- Kelly, T. M., & Daley, D. C. (2013). Integrated treatment of substance use and psychiatric disorders. *Social Work in Public Health*, 28(3–4), 388–406.
- Kerner, B. (2015). Comorbid substance use disorders in schizophrenia: A latent class approach. *Psychiatry Research*, 225(3), 395–401.
- Kerridge, B. T., Chou, S. P., Pickering, R. P., Ruan, W. J., Huang, B., Jung, J., ... Hasin, D. S. (2019). Changes in the prevalence and correlates of cocaine use and cocaine use disorder in the United States, 2001–2002 and 2012–2013. *Addictive Behaviors*, 90, 250–257.
- Kesby, J. P., Eyles, D. W., McGrath, J. J., & Scott, J. G. (2018). Dopamine, psychosis and schizophrenia: The widening gap between basic and clinical neuroscience. *Translational Psychiatry*, 8(1), 1–12.
- Kessler, R. C., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Wittchen, H. U. (2012). Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *International Journal of Methods in Psychiatric Research*, 21(3), 169–184.
- Keuroghlian, A. S., Reisner, S. L., White, J. M., & Weiss, R. D. (2015). Substance use and treatment of substance use disorders in a community sample of transgender adults. *Drug and Alcohol Dependence*, 152, 139–146.
- Kevil, C. G., Goeders, N. E., Woolard, M. D., Bhuiyan, M. S., Dominic, P., Kolluru, G. K., ... Orr, A. W. (2019). Methamphetamine use and cardiovascular disease. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 39(9), 1739–1746.
- Kidd, J. D., Goetz, T. G., Shea, E. A., & Bockting, W. O. (2021). Prevalence and minority-stress correlates of past 12-month prescription drug misuse in a national sample of transgender and gender nonbinary adults: Results from the US Transgender Survey. *Drug and Alcohol Dependence*, 219, 108474.
- Kiluk, B. D., Babuscio, T. A., Nich, C., & Carroll, K. M. (2013). Smokers versus snorters: Do treatment outcomes differ according to route of cocaine administration? *Experimental and Clinical Psychopharmacology*, 21(6), 490–498.
- Kilwein, T. M., Goodman, E. L., Looby, A., & De Young, K. P. (2016). Nonmedical prescription stimulant use for suppressing appetite and controlling body weight is uniquely associated with more severe eating disorder symptomatology. *International Journal of Eating Disorders*, 49(8), 813–816.
- Kim, D. (2021, April 1). Too well-off to seek help?: The model minority myth of Asian Americans [Blog post]. <https://adaa.org/learn-from-us/from-the-experts/blog-posts/professional/too-well-seek-help-model-minority-myth-asian>
- Kim, S. T., & Park, T. (2019). Acute and chronic effects of cocaine on cardiovascular health. *International Journal of Molecular Sciences*, 20(3), 584.
- Kimbrough, A., Smith, L. C., Kallupi, M., Simpson, S., Collazo, A., & George, O. (2019). Characterization of the brain functional architecture of psychostimulant withdrawal using single-cell whole brain imaging. *bioRxiv*. doi:10.1101/743799
- King, K. A., Vidourek, R. A., & Yockey, R. A. (2019). Social determinants to lifetime methamphetamine use among a national sample of adults. *Journal of Substance Use*, 24(4), 388–393.

- Kirby, K. C., Benishek, L. A., & Tabit, M. B. (2016). Contingency management works, clients like it, and it is cost-effective. *American Journal of Drug and Alcohol Abuse*, 42(3), 250–253.
- Kirby, K. C., Carpenedo, C. M., Dugosh, K. L., Rosenwasser, B. J., Benishek, L. A., Janik, A., ... Silverman, K. (2013). Randomized clinical trial examining duration of voucher-based reinforcement therapy for cocaine abstinence. *Drug and Alcohol Dependence*, 132(3), 639–645.
- Kish, S. J., Boileau, I., Callaghan, R. C., & Tong, J. (2017). Brain dopamine neurone 'damage': Methamphetamine users vs. Parkinson's disease; A critical assessment of the evidence. *European Journal of Neuroscience*, 45(1), 58–66.
- Kittirattanapaiboon, P., Srikosai, S., & Wittayanookulluk, A. (2017). Methamphetamine use and dependence in vulnerable female populations. *Current Opinion in Psychiatry*, 30(4), 247–252.
- Kiyatkin, E. A. (2019). Respiratory depression and brain hypoxia induced by opioid drugs: Morphine, oxycodone, heroin, and fentanyl. *Neuropharmacology*, 151, 219–226.
- Klassen, L. J., Bilkey, T. S., Katzman, M. A., & Chokka, P. (2012). Comorbid attention deficit/hyperactivity disorder and substance use disorder: Treatment considerations. *Current Drug Abuse Reviews*, 5(3), 190–198.
- Klega, A. E., & Keehbauch, J. T. (2018). Stimulant and designer drug use: Primary care management. *American Family Physician*, 98(2), 85–92.
- Klein, M. O., Battagello, D. S., Cardoso, A. R., Hauser, D. N., Bittencourt, J. C., & Correa, R. G. (2019). Dopamine: Functions, signaling, and association with neurological diseases. *Cellular and Molecular Neurobiology*, 39(1), 31–59.
- Klevens, R. M., Hu, D. J., Jiles, R., & Holmberg, S. D. (2012). Evolving epidemiology of hepatitis C virus in the United States. *Clinical Infectious Diseases*, 55(Suppl. 1), S3–S9.
- Kleykamp, B. A., Guille, C., Barth, K. S., & McClure, E. A. (2020). Substance use disorders and COVID-19: The role of telehealth in treatment and research. *Journal of Social Work Practice in the Addictions*, 20(3), 248–253.
- Kloss, B. T., Broton, C. E., & Rodriguez, E. (2010). Pneumomediastinum from nasal insufflation of cocaine. *International Journal of Emergency Medicine*, 3, 435–437.
- Klostermann, K., Kelley, M. L., Mignone, T., Pusateri, L., & Wills, K. (2011). Behavioral couples therapy for substance abusers: Where do we go from here? *Substance Use and Misuse*, 46(12), 1502–1509.
- Knapp, W. P., Soares, B. G., Farrel, M., & Lima, M. S. (2007). Psychosocial interventions for cocaine and psychostimulant amphetamines related disorders. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.CD003023.pub2
- Knight, K. (2020). Structural factors that affect life contexts of pregnant people with opioid use disorders: The role of structural racism and the need for structural competency. *Women's Reproductive Health*, 7, 164–171.
- Kober, H. H. (2014). Emotion regulation in substance use disorders. In J. J. Gross (Ed.), *Handbook of emotion regulation* (pp. 428–446). Guilford Press.
- Komaromy, M., Mendez-Escobar, E., & Madden, E. (2021). Addressing racial trauma in the treatment of substance use disorders. *Pediatrics*, 147(Suppl. 2), S268–S270.
- Koob, G. F., & Volkow, N. D. (2016). Neurobiology of addiction: A neurocircuitry analysis. *Lancet Psychiatry*, 3(8), 760–773.
- Köpetz, C. E., Lejuez, C. W., Wiers, R. W., & Kruglanski, A. W. (2013). Motivation and self-regulation in addiction: A call for convergence. *Perspectives on Psychological Science*, 8(1), 3–24.
- Kousik, S. M., Napier, T. C., & Carvey, P. M. (2012). The effects of psychostimulant drugs on blood brain barrier function and neuroinflammation. *Frontiers in Pharmacology*, 3, 121.
- Krakowski, A., & Ickowicz, A. (2018). Stimulant withdrawal in a child with autism spectrum disorder and ADHD: A case report. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, 27(2), 148–151.
- Kral, A. H., Lambdin, B. H., Comfort, M., Powers, C., Cheng, H., Lopez, A. M., ... Lorvick, J. (2018). A strengths-based case management intervention to reduce HIV viral load among people who use drugs. *AIDS and Behavior*, 22(1), 146–153.
- Krans, E. E., Bogen, D., Richardson, G., Park, S. Y., Dunn, S. L., & Day, N. (2016). Factors associated with buprenorphine versus methadone use in pregnancy. *Substance Abuse*, 37(4), 550–557.
- Kreek, M. J., Levran, O., Reed, B., Schlussman, S. D., Zhou, Y., & Butelman, E. R. (2012). Opiate addiction and cocaine addiction: Underlying molecular neurobiology and genetics. *Journal of Clinical Investigation*, 122(10), 3387–3393.
- Kruse, C. S., Lee, K., Watson, J. B., Lobo, L. G., Stoppelmoor, A. G., & Oyibo, S. E. (2020). Measures of effectiveness, efficiency, and quality of telemedicine in the management of alcohol abuse, addiction, and rehabilitation: A systematic review. *Journal of Medical Internet Research*, 22(1), e13252.
- Kuczyńska, K., Grzonkowski, P., Kacprzak, Ł., & Zawilska, J. B. (2018). Abuse of fentanyl: An emerging problem to face. *Forensic Science International*, 289, 207–214.
- Kunins, H. V. (2020). Structural racism and the opioid overdose epidemic: The need for antiracist public health practice. *Journal of Public Health Management and Practice*, 26(3), 201–205.



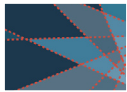
- Kuper, L. E., Nussbaum, R., & Mustanski, B. (2012). Exploring the diversity of gender and sexual orientation identities in an online sample of transgender individuals. *Journal of Sex Research, 49*(2–3), 244–254.
- Kuypers, K., Verkes, R. J., van den Brink, W., van Amsterdam, J., & Ramaekers, J. G. (2020). Intoxicated aggression: Do alcohol and stimulants cause dose-related aggression? A review. *European Neuropsychopharmacology, 30*, 114–147.
- LaBelle, C. T., Han, S. C., Bergeron, A., & Samet, J. H. (2016). Office-based opioid treatment with buprenorphine (OBOT-B): Statewide implementation of the Massachusetts Collaborative Care Model in community health centers. *Journal of Substance Abuse Treatment, 60*, 6–13.
- LaFromboise, T. D., Hoyt, D. R., Oliver, L., & Whitbeck, L. B. (2006). Family, community, and school influences on resilience among American Indian adolescents in the upper Midwest. *Journal of Community Psychology, 34*(2), 193–209.
- Lagisetty, P., Klasa, K., Bush, C., Heisler, M., Chopra, V., & Bohnert, A. (2017). Primary care models for treating opioid use disorders: What actually works? A systematic review. *PLoS One, 12*(10), e0186315.
- Lakhan, S. E., & Kirchgessner, A. (2012). Prescription stimulants in individuals with and without attention deficit hyperactivity disorder: Misuse, cognitive impact, and adverse effects. *Brain and Behavior, 2*(5), 661–677.
- Lameijer, H., Azizi, N., Ligtenberg, J. J. M., & Ter Maaten, J. C. (2014). Ventricular tachycardia after naloxone administration: A drug related complication? Case report and literature review. *Drug Safety–Case Reports, 1*, 2.
- Lander, L., Howsare, J., & Byrne, M. (2013). The impact of substance use disorders on families and children: From theory to practice. *Social Work in Public Health, 28*(3–4), 194–205.
- Lannett Company. (2020). *Numbrino: Highlights of prescribing information*. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/209575s000lbl.pdf
- Lansky, A., Finlayson, T., Johnson, C., Holtzman, D., Wejnert, C., Mitsch, A., ... Crepaz, N. (2014). Estimating the number of persons who inject drugs in the United States by meta-analysis to calculate national rates of HIV and hepatitis C virus infections. *PLoS One, 9*(5), e97596.
- Lappan, S. N., Brown, A. W., & Hendricks, P. S. (2020). Dropout rates of in-person psychosocial substance use disorder treatments: A systematic review and meta-analysis. *Addiction, 115*(20), 201–217.
- Lappin, J. M., Darke, S., & Farrell, M. (2017). Stroke and methamphetamine use in young adults: A review. *Journal of Neurology, Neurosurgery, and Psychiatry, 88*(12), 1079–1091.
- Lappin, J. M., Darke, S., & Farrell, M. (2018). Methamphetamine use and future risk for Parkinson's disease: Evidence and clinical implications. *Drug and Alcohol Dependence, 187*, 134–140.
- Lappin, J. M., & Sara, G. E. (2019). Psychostimulant use and the brain. *Addiction, 114*(11), 2065–2077.
- LaRue, L., Twillman, R. K., Dawson, E., Whitley, P., Frasco, M. A., Huskey, A., & Guevara, M. G. (2019). Rate of fentanyl positivity among urine drug test results positive for cocaine or methamphetamine. *JAMA Network Open, 2*(4), e192851.
- Lawn, W., Aldridge, A., Xia, R., & Winstock, A. R. (2019). Substance-linked sex in heterosexual, homosexual, and bisexual men and women: An online, cross-sectional "global drug survey" report. *Journal of Sexual Medicine, 16*(5), 721–732.
- LeardMann, C. A., McMaster, H. S., Warner, S., Esquivel, A. P., Porter, B., Powell, T. M., ... Millennium Cohort Study Team. (2021). Comparison of posttraumatic stress disorder checklist instruments from *Diagnostic and Statistical Manual of Mental Disorders*, vs Fifth Edition in a large cohort of US Military service members and veterans. *JAMA Network Open, 4*(4), e218072–e218072.
- Lecomte, T., Dumais, A., Dugré, J. R., & Potvin, S. (2018). The prevalence of substance-induced psychotic disorder in methamphetamine misusers: A meta-analysis. *Psychiatry Research, 268*, 189–192.
- Lee, N. K., Jenner, L., Harney, A., & Cameron, J. (2018). Pharmacotherapy for amphetamine dependence: A systematic review. *Drug and Alcohol Dependence, 191*, 309–337.
- Lenz, A. S., Henesy, R., & Callender, K. (2016). Effectiveness of Seeking Safety for co-occurring posttraumatic stress disorder and substance use. *Journal of Counseling and Development, 94*(1), 51–61.
- Lerner, A., & Klein, M. (2019). Dependence, withdrawal and rebound of CNS drugs: An update and regulatory considerations for new drugs development. *Brain Communications, 1*(1), fcz025.
- Levin, F. R., Mariani, J. J., Specker, S., Mooney, M., Mahony, A., Brooks, D. J., ... Grabowski, J. (2015). Extended-release mixed amphetamine salts vs placebo for comorbid adult attention-deficit/hyperactivity disorder and cocaine use disorder: A randomized clinical trial. *JAMA Psychiatry, 72*(6), 593–602.
- Lewis, D. A., Park, J. N., Vail, L., Sine, M., Welsh, C., & Sherman, S. G. (2016). Evaluation of the Overdose Education and Naloxone Distribution Program of the Baltimore Student Harm Reduction Coalition. *American Journal of Public Health, 106*(7), 1243–1246.
- Lewis, K., & O'Day, C. S. (2020). Dystonic reactions. In *StatPearls*. <https://www.ncbi.nlm.nih.gov/books/NBK531466/>

- Li, L., Sujan, A. C., Butwicka, A., Chang, Z., Cortese, S., Quinn, P., ... Larsson, H. (2020). Associations of prescribed ADHD medication in pregnancy with pregnancy-related and offspring outcomes: A systematic review. *CNS Drugs*, 34(7), 731–747.
- Li, W., & Pozzo-Miller, L. (2020). Dysfunction of the corticostriatal pathway in autism spectrum disorders. *Journal of Neuroscience Research*, 98(11), 2130–2147.
- Lin, L. A., Fernandez, A. C., & Bonar, E. E. (2020). Telehealth for substance-using populations in the age of coronavirus disease 2019: Recommendations to enhance adoption. *JAMA Psychiatry*, 77(12), 1209–1210.
- Lindson, N., Thompson, T. P., Ferrey, A., Lambert, J. D., & Aveyard, P. (2019). Motivational interviewing for smoking cessation. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.CD006936.pub4
- Linton, S. L., Celentano, D. D., Kirk, G. D., & Mehta, S. H. (2013). The longitudinal association between homelessness, injection drug use, and injection-related risk behavior among persons with a history of injection drug use in Baltimore, MD. *Drug and Alcohol Dependence*, 132(3), 457–465.
- Liu, Y., Williamson, V., Setlow, B., Cottler, L. B., & Knackstedt, L. A. (2018). The importance of considering polysubstance use: Lessons from cocaine research. *Drug and Alcohol Dependence*, 192, 16–28.
- Lokoff, A., & Maynes, J. T. (2019). The incidence, significance, and management of accidental intra-arterial injection: A narrative review. *Canadian Journal of Anesthesia*, 66(5), 576–592.
- Longheu, A., Medas, F., Corrias, F., Farris, S., Tatti, A., Pisano, G., ... Calò, P. G. (2016). Surgical management of gynecomastia: Experience of a general surgery center. *Il Giornale di Chirurgia*, 37(4), 150–154.
- López-Núñez, C., Alonso-Pérez, F., Pedrosa, I., & Secades-Villa, R. (2016). Cost-effectiveness of a voucher-based intervention for smoking cessation. *American Journal of Drug and Alcohol Abuse*, 42(3), 296–305.
- Lopez-Patton, M., Kumar, M., Jones, D., Fonseca, M., Kumar, A. M., & Nemeroff, C. B. (2016). Childhood trauma and METH abuse among men who have sex with men: Implications for intervention. *Journal of Psychiatric Research*, 72, 1–5.
- Lorenzetti, V. (2018, August 13–15). *Neural pathways in gambling and cocaine use disorders: Commonalities and differences from neuroimaging study* [Paper presentation]. Gambling Harm 2018: Taking Action for Change, Geelong, Victoria, Australia.
- Loza, O., Curiel, Z. V., Beltran, O., & Ramos, R. (2020). Methamphetamine use and sexual risk behaviors among men who have sex with men in a Mexico-US border city. *American Journal on Addictions*, 29(2), 111–119.
- Lusk, S. L., & Veale, F. R. (2018). Increasing successful vocational rehabilitation outcomes for individuals with substance use disorders. *Journal of Applied Rehabilitation Counseling*, 49(1), 4–10.
- Lutnick, A., Harris, J., Lorvick, J., Cheng, H., Wenger, L. D., Bourgois, P., & Kral, A. H. (2015). Examining the associations between sex trade involvement, rape, and symptomatology of sexual abuse trauma. *Journal of Interpersonal Violence*, 30(11), 1847–1863.
- Lyons, T., Chandra, G., Goldstein, J., & Ostrow, D. G. (2010). Breaking the bond between stimulant use and risky sex: A qualitative study. *Substance Abuse*, 31(4), 224–230.
- Ma, T., Sun, Y., & Ku, Y. (2019). Effects of non-invasive brain stimulation on stimulant craving in users of cocaine, amphetamine, or methamphetamine: A systematic review and meta-analysis. *Frontiers in Neuroscience*, 13, 1095.
- Maagdenberg, T., Savci, S., & Iffy, L. (2006). Cocaine intoxication mimicking preeclampsia postpartum. *International Journal of Gynaecology and Obstetrics*, 92(1), 73–74.
- MacArthur, G. J., van Velzen, E., Palmateer, N., Kimber, J., Pharris, A., Hope, V., ... Hutchinson, S. J. (2014). Interventions to prevent HIV and hepatitis C in people who inject drugs: A review of reviews to assess evidence of effectiveness. *International Journal on Drug Policy*, 25(1), 34–52.
- MacLean, R. R., & Sofuoglu, M. (2018). Stimulants and mood disorders. *Current Addiction Reports*, 5, 323–329.
- MacNeil, J., & Pauly, B. (2011). Needle exchange as a safe haven in an unsafe world. *Drug and Alcohol Review*, 30(1), 26–32.
- MacNicol, B. (2017). The biology of addiction. *Canadian Journal of Anaesthesia*, 64(2), 141–148.
- Magidson, J. F., Liu, S. M., Lejuez, C. W., & Blanco, C. (2012). Comparison of the course of substance use disorders among individuals with and without generalized anxiety disorder in a nationally representative sample. *Journal of Psychiatric Research*, 46(5), 659–666.
- Mahoney, J. J., III. (2019). Cognitive dysfunction in individuals with cocaine use disorder: Potential moderating factors and pharmacological treatments. *Experimental and Clinical Psychopharmacology*, 27(3), 203–214.
- Mahoney, M. C., Erwin, D. O., Twarozek, A. M., Saad-Harfouche, F. G., Rodriguez, E. M., Sun, X., ... Fox, C. (2018). Leveraging technology to promote smoking cessation in urban and rural primary care medical offices. *Preventative Medicine*, 114, 102–106.
- Maia, A., Martins, F. T., Silva Neto, L. D., Alves, R. B., & De Fátima, Á. (2017). Cocaethylene, the in vivo product of cocaine and ethanol, is a narcotic more potent than its precursors. *Acta Crystallographica, Section C, Structural Chemistry*, 73(Pt. 10), 780–783.



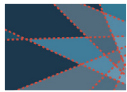
- Maiorana, A., Kegeles, S. M., Brown, S., Williams, R., & Arnold, E. A. (2021). Substance use, intimate partner violence, history of incarceration and vulnerability to HIV among young Black men who have sex with men in a Southern US city. *Culture, Health and Sexuality*, 23(1), 37–51.
- Malcolm, R., Barth, K. S., & Veatch, L. M. (2013). Cocaine addiction. In P. M. Miller (Ed.), *Principles of addiction* (pp. 669–678). Academic Press.
- Maloney, W. J. (2010). The significance of cocaine use to dental practice. *New York State Dental Journal*, 76(6), 36–39.
- Mangado, E. O., & Madoz-Gúrpide, A. (2009). Is the capacity of forming abstract concepts affected by cocaine use? Application of Wisconsin Test in a prospective study. *European Psychiatry*, 24(S1), 1.
- Mariotti, K. C., Rossato, L. G., Fröhlich, P. E., & Limberger, R. P. (2013). Amphetamine-type medicines: A review of pharmacokinetics, pharmacodynamics, and toxicological aspects. *Current Clinical Pharmacology*, 8(4), 350–357.
- Markowitz, J. S., & Patrick, K. S. (2017). The clinical pharmacokinetics of amphetamines utilized in the treatment of attention-deficit/hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology*, 27(8), 678–689.
- Marlatt, G. A., & Gordon, J. R. (1985). *Relapse prevention*. Guilford Press.
- Marquez, C., Mitchell, S. J., Hare, C. B., John, M., & Klausner, J. D. (2009). Methamphetamine use, sexual activity, patient–provider communication, and medication adherence among HIV-infected patients in care, San Francisco 2004–2006. *AIDS Care*, 21(5), 575–582.
- Marraccini, M. E., Weyandt, L. L., Gudmundsdottir, B. G., Oster, D. R., & McCallum, A. (2017). Attention–deficit hyperactivity disorder: Clinical considerations for women. *Journal of Midwifery and Women's Health*, 62(6), 684–695.
- Marraccini, M. E., Weyandt, L. L., Rossi, J. S., & Gudmundsdottir, B. G. (2016). Neurocognitive enhancement or impairment? A systematic meta-analysis of prescription stimulant effects on processing speed, decision-making, planning, and cognitive perseveration. *Experimental and Clinical Psychopharmacology*, 24(4), 269–284.
- Marschall-Lévesque, S., Castellanos-Ryan, N., Parent, S., Renaud, J., Vitaro, F., Boivin, M., ... Séguin, J. R. (2017). Victimization, suicidal ideation, and alcohol use from age 13 to 15 years: Support for the self-medication model. *Journal of Adolescent Health*, 60(4), 380–387.
- Marshall, B. D., & Werb, D. (2010). Health outcomes associated with methamphetamine use among young people: A systematic review. *Addiction*, 105(6), 991–1002.
- Martin, C. E., Scialli, A., & Terplan, M. (2020). Unmet substance use disorder treatment need among reproductive age women. *Drug and Alcohol Dependence*, 206, 107679.
- Mash, D. C. (2016). Excited delirium and sudden death: A syndromal disorder at the extreme end of the neuropsychiatric continuum. *Frontiers in Physiology*, 7, 435.
- Maslow, A. H. (1943). A theory of human motivation. *Psychological Review*, 50, 370–396.
- Masson, C. L., Shopshire, M. S., Sen, S., Hoffman, K., Hengl, N., Bartolome J., ... Iguchi, M. (2013). Possible barriers to enrollment in substance abuse treatment among a diverse sample of Asian Americans and Pacific Islanders: Opinions of treatment clients. *Journal of Substance Abuse Treatment*, 44(3), 309–315.
- Mastro, T. D., Akolo, C., & Shoptaw, S. (2020). Managing amphetamine use is critical to achieving HIV control. *AIDS*, 34(13), 1971–1973.
- Matsumoto, R. R., Seminerio, M. J., Turner, R. C., Robson, M. J., Nguyen, L., Miller, D. B., & O'Callaghan, J. P. (2014). Methamphetamine-induced toxicity: An updated review on issues related to hyperthermia. *Pharmacology and Therapeutics*, 144(1), 28–40.
- Matsuzaka, S. (2018). Transgressing gender norms in addiction treatment: Transgender rights to access within gender-segregated facilities. *Journal of Ethnicity in Substance Abuse*, 17(4), 420–433.
- Maxwell, J. C. (2014). A new survey of methamphetamine users in treatment: Who they are, why they like “meth,” and why they need additional services. *Substance Use and Misuse*, 49(6), 639–644.
- Maxwell, S., Gafos, M., Moncrieff, M., Shahmanesh, M., & Stirrup, O. (2020). Pre-exposure prophylaxis use among men who have sex with men who have experienced problematic chemsex. *International Journal of STD and AIDS*, 31(5), 474–480.
- Maxwell, S., Shahmanesh, M., & Gafos, M. (2019). Chemsex behaviours among men who have sex with men: A systematic review of the literature. *International Journal of Drug Policy*, 63, 74–89.
- Mayer, K. H., Agwu, A., & Malebranche, D. (2020). Barriers to the wider use of pre-exposure prophylaxis in the United States: A narrative review. *Advances in Therapy*, 37(5), 1778–1811.
- Mayer, K. H., Jones, D., Oldenburg, C., Jain, S., Gelman, M., Zaslow, S., ... Mimiaga, M. J. (2017). Excellent HIV post-exposure prophylaxis regimen completion with single tablet daily elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine compared with more frequent dosing regimens. *Journal of Acquired Immune Deficiency Syndromes*, 75(5), 535–539.

- Mayo Clinic. (2017a, September 1). Transgender facts. <https://www.mayoclinic.org/healthy-lifestyle/adult-health/in-depth/transgender-facts/art-20266812>
- Mayo Clinic. (2017b, December 22). Aortic dissection. <https://www.mayoclinic.org/diseases-conditions/aortic-dissection/symptoms-causes/syc-20369496>
- Mayo Clinic. (2018, October 19). Prescription drug abuse. <https://www.mayoclinic.org/diseases-conditions/prescription-drug-abuse/symptoms-causes/syc-20376813>
- Mayo Clinic. (2020, January 18). Placental abruption. <https://www.mayoclinic.org/diseases-conditions/placental-abruption/symptoms-causes/syc-20376458>
- McCabe, S. E., & West, B. T. (2013). Medical and nonmedical use of prescription stimulants: Results from a national multicohort study. *Journal of the American Academy of Child and Adolescent Psychiatry*, 52(12), 1272–1280.
- McCall Jones, C., Baldwin, G. T., & Compton, W. M. (2017). Recent increases in cocaine-related overdose deaths and the role of opioids. *American Journal of Public Health*, 107(3), 430–432.
- McCarthy, E., & McClain, E. (2019). Methamphetamine-induced lung injury. *European Journal of Case Reports in Internal Medicine*, 6(6).
- McDonell, M. G., Srebnik, D., Angelo, F., McPherson, S., Lowe, J. M., Sugar, A., ... Ries, R. K. (2013). Randomized controlled trial of contingency management for stimulant use in community mental health patients with serious mental illness. *American Journal of Psychiatry*, 170(1), 94–101.
- McGowan, C. E., & Fried, M. W. (2012). Barriers to hepatitis C treatment. *Liver International*, 32(Suppl. 1), 151–156.
- McHugh, R. K. (2015). Treatment of co-occurring anxiety disorders and substance use disorders. *Harvard Review of Psychiatry*, 23(2), 99–111.
- McHugh, R. K., Hearon, B. A., & Otto, M. W. (2010). Cognitive behavioral therapy for substance use disorders. *Psychiatric Clinics*, 33(3), 511–525.
- McHugh, R. K., Hu, M. C., Campbell, A. N., Hilario, E. Y., Weiss, R. D., & Hien, D. A. (2014). Changes in sleep disruption in the treatment of co-occurring posttraumatic stress disorder and substance use disorders. *Journal of Traumatic Stress*, 27(1), 82–89.
- McKay, J. R. (2017). Making the hard work of recovery more attractive for those with substance use disorders. *Addiction*, 112(5), 751–757.
- McKenna, S. A. (2013). “We’re supposed to be asleep?” Vigilance, paranoia, and the alert methamphetamine user. *Anthropology of Consciousness*, 24(2), 172–190.
- McKetin, R. (2018). Methamphetamine psychosis: Insights from the past. *Addiction*, 113(8), 1522–1527.
- McKetin, R., Boden, J. M., Foulds, J. A., Najman, J. M., Ali, R., Degenhardt, L., ... Weatherburn, D. (2020). The contribution of methamphetamine use to crime: Evidence from Australian longitudinal data. *Drug and Alcohol Dependence*, 216, 108262.
- McKetin, R., Lubman, D. I., Baker, A., Dawe, S., Ross, J., Mattick, R. P., & Degenhardt, L. (2018). The relationship between methamphetamine use and heterosexual behaviour: Evidence from a prospective longitudinal study. *Addiction*, 113(7), 1276–1285.
- McKetin, R., Lubman, D. I., Najman, J. M., Dawe, S., Butterworth, P., & Baker, A. L. (2014). Does methamphetamine use increase violent behaviour? Evidence from a prospective longitudinal study. *Addiction*, 109(5), 798–806.
- Mee-Lee, D., & Shulman, G. D. (2009). The ASAM placement criteria and matching patients to treatment. In R. K. Ries, S. Miller, D. A. Fiellin, & R. Saitz (Eds.), *Principles of addiction medicine* (4th ed., pp. 387–399). Lippincott Williams & Wilkins.
- Mee-Lee, D., Shulman, G. D., Fishman, M. J., Gastfriend, D. R., & Miller, M. M., (Eds.). (2013). *The ASAM criteria: Treatment criteria for addictive, substance-related, and co-occurring conditions* (3rd ed.). The Change Companies.
- Mégarbane, B., & Chevillard, L. (2013). The large spectrum of pulmonary complications following illicit drug use: Features and mechanisms. *Chemico-Biological Interactions*, 206(3), 444–451.
- Meier, S. C., & Labuski, C. M. (2013). The demographics of the transgender population. In A. K. Baumle (Ed.), *International handbook of the demography of sexuality* (pp. 289–327). Springer Science.
- Merriam-Webster. (n.d.-a). End organ. In *Merriam-Webster.com dictionary*. Retrieved March 19, 2021, from <https://www.merriam-webster.com/dictionary/end%20organ>
- Merriam-Webster. (n.d.-b). Sensorium. In *Merriam-Webster.com dictionary*. Retrieved March 19, 2021, from <https://www.merriam-webster.com/dictionary/sensorium>
- Mesa, F., Le, T.-A., & Beidel, D. (2015). Social skill-based treatment for social anxiety disorder in adolescents. In K. Ranta, A. M. La Greca, L.-J. Garcia-Lopez, & M. Marttunen (Eds.), *Social anxiety and phobia in adolescent: Development, manifestation and intervention strategies* (pp. 289–299). Springer International Publishing.
- Mete, M., Sakoglu, U., Spence, J. S., Devous, M. D., Sr., Harris, T. S., & Adinoff, B. (2016). Successful classification of cocaine dependence using brain imaging: A generalizable machine learning approach. *BMC Bioinformatics*, 17(Suppl. 13), 357.
- Metzl, J., & Roberts, D. (2014). Structural competency meets structural racism: Race, politics, and the structure of medical knowledge. *Virtual Mentor*, 16, 674–690.



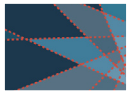
- Meyers, R. J., Roozen, H. G., & Smith, J. E. (2011). The community reinforcement approach: An update of the evidence. *Alcohol Research and Health*, 33(4), 380–388.
- Meyers, R. J., & Smith, J. E. (1995). *Clinical guide to alcohol treatment: The community reinforcement approach*. Guilford Press.
- Miguel, A. Q., Kiluk, B. D., Roos, C. R., Babuscio, T. A., Nich, C., Mari, J. J., & Carroll, K. M. (2019). Change in employment status and cocaine use treatment outcomes: A secondary analysis across six clinical trials. *Journal of Substance Abuse Treatment*, 106, 89–96.
- Miller, W. R. (1985). Motivation for treatment: A review with special emphasis on alcoholism. *Psychological Bulletin*, 98, 84–107.
- Miller, W. R. (1995). Increasing motivation for change. In R. K. Hester & W. R. Miller (Eds.), *Handbook of alcoholism treatment approaches: Effective alternatives* (2nd ed., pp. 89–104). Allyn & Bacon.
- Miller, W. R., & Rollnick, S. (1991). *Motivational interviewing: Preparing people to change addictive behavior*. Guilford Press.
- Mimiaga, M. J., Pantalone, D. W., Biello, K. B., Glynn, T. R., Santostefano, C. M., Olson, J., ... Safren, S. A. (2018). A randomized controlled efficacy trial of behavioral activation for concurrent stimulant use and sexual risk for HIV acquisition among MSM: Project IMPACT study protocol. *BMC Public Health*, 18, 914.
- Min, S. Y., Whitecraft, J., Rothbard, A. B., & Salzer, M. S. (2007). Peer support for persons with co-occurring disorders and community tenure: A survival analysis. *Psychiatric Rehabilitation Journal*, 30, 207–213.
- Minnes, S., Min, M. O., Singer, L. T., Edguer, M., Wu, M., & Thi, P. (2012). Cocaine use during pregnancy and health outcome after 10 years. *Drug and Alcohol Dependence*, 126(1–2), 71–79.
- Minozzi, S., Saulle, R., De Crescenzo, F., & Amato, L. (2016). Psychosocial interventions for psychostimulant misuse. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.CD011866.pub2
- Mitchell, O., Wilson, D. B., & MacKenzie, D. L. (2012). The effectiveness of incarceration-based drug treatment on criminal behavior: A systematic review. *Campbell Systematic Reviews*, 8(1), i–76.
- Moeller, K. E., Kissack, J. C., Atayee, R. S., & Lee, K. C. (2017). Clinical interpretation of urine drug tests: What clinicians need to know about urine drug screens. *Mayo Clinic Proceedings*, 92(5), 774–796.
- Moeller, S. J., & Paulus, M. P. (2018). Toward biomarkers of the addicted human brain: Using neuroimaging to predict relapse and sustained abstinence in substance use disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 80(Pt. B), 143–154.
- Molina, B. S. G., & Swanson, J. M. (2020). Why are long-term benefits of stimulant medication so difficult to detect? *ADHD Report*, 28(1), 1–7.
- Moody, R. L., Starks, T. J., Grov, C., & Parsons, J. T. (2018). Internalized homophobia and drug use in a national cohort of gay and bisexual men: Examining depression, sexual anxiety, and gay community attachment as mediating factors. *Archives of Sexual Behavior*, 47(4), 1133–1144.
- Morais, A., Pita, I. R., Fontes-Ribeiro, C. A., & Pereira, F. C. (2018). The neurobiological mechanisms of physical exercise in methamphetamine addiction. *CNS Neuroscience and Therapeutics*, 24(2), 85–97.
- Moran, L. V., Ongur, D., Hsu, J., Castro, V. M., Perlis, R. H., & Schneeweiss, S. (2019). Psychosis with methylphenidate or amphetamine in patients with ADHD. *New England Journal of Medicine*, 380(12), 1128–1138.
- Moreno-Rius, J., & Miquel, M. (2017). The cerebellum in drug craving. *Drug and Alcohol Dependence*, 173, 151–158.
- Morgenstern, J., Hogue, A., Dauber, S., Dasaro, C., & McKay, J. R. (2009). Does coordinated care management improve employment for substance-using welfare recipients? *Journal of Studies on Alcohol and Drugs*, 70(6), 955–963.
- Morris, L., Stander, J., Ebrahim, W., Eksteen, S., Meaden, O. A., Ras, A., & Wessels, A. (2018). Effect of exercise versus cognitive behavioural therapy or no intervention on anxiety, depression, fitness, and quality of life in adults with previous methamphetamine dependency: A systematic review. *Addiction Science and Clinical Practice*, 13(1), 4.
- Moss, M. J., Hendrickson, R. G., & Toxicology Investigators Consortium (ToxIC). (2019). Serotonin toxicity: Associated agents and clinical characteristics. *Journal of Clinical Psychopharmacology*, 39(6), 628–633.
- Mueller, M. D., & Wyman, J. R. (1997). Study sheds new light on the state of drug abuse treatment nationwide. *NIDA Notes*, 12(5), 1–7.
- Müller, C. P., & Homberg, J. R. (2015). The role of serotonin in drug use and addiction. *Behavioural Brain Research*, 277, 146–192.
- Munro, B. A., Weyandt, L. L., Marraccini, M. E., & Oster, D. R. (2017). The relationship between nonmedical use of prescription stimulants, executive functioning and academic outcomes. *Addictive Behaviors*, 65, 250–257.
- Murch, D. (2015). Crack in Los Angeles: Crisis, militarization, and Black response to the late twentieth-century war on drugs. *Journal of American History*, 102(1), 162–173.
- Murphy, S. M., Campbell, A. N. C., Ghitza, U. E., Kyle, T. L., Bailey, G. L., Nunes, E. V., & Polsky, D. (2016). Cost-effectiveness of an internet-delivered treatment for substance abuse: Data from a multisite randomized controlled trial. *Drug and Alcohol Dependence*, 161, 119–126.

- Nakamura, N., Mausbach, B. T., Ulibarri, M. D., Semple, S. J., & Patterson, T. L. (2011). Methamphetamine use, attitudes about condoms, and sexual risk behavior among HIV-positive men who have sex with men. *Archives of Sexual Behavior*, 40(2), 267–272.
- Nash, A. J. (2020). The twelve steps and adolescent recovery: A concise review. *Substance Abuse: Research and Treatment*, 14, 1178221820904397.
- Nassar, P., & Ouanounou, A. (2020). Cocaine and methamphetamine: Pharmacology and dental implications. *Canadian Journal of Dental Hygiene*, 54(2), 75–82.
- National Academies of Sciences, Engineering, and Medicine. (2016). *Ending discrimination against people with mental and substance use disorders: The evidence for stigma change* (p. 23442). National Academies Press.
- National Center for Biotechnology Information. (2021). PubChem compound summary for CID 446220, cocaine. Retrieved March 22, 2021, from <https://pubchem.ncbi.nlm.nih.gov/compound/Cocaine>
- National Center for Health Statistics. (2020). About multiple cause of death, 1999–2019. *CDC WONDER*. Centers for Disease Control and Prevention. Retrieved March 25, 2021, through <https://wonder.cdc.gov/mcd-icd10.html>
- National Institute on Drug Abuse. (2014). *Stimulant ADHD medications: Methylphenidate and amphetamines DrugFacts*. National Institutes of Health.
- National Institute on Drug Abuse (2015). *Therapeutic communities* (NIH Publication Number 15-4877). National Institutes of Health.
- National Institute on Drug Abuse. (2016a). *Cocaine research report*. National Institutes of Health.
- National Institute on Drug Abuse. (2016b, May). What are the effects of maternal cocaine use? <https://www.drugabuse.gov/publications/research-reports/cocaine/what-are-effects-maternal-cocaine-use>
- National Institute on Drug Abuse. (2016c, May). Why are cocaine users at risk for contracting HIV/AIDS and hepatitis? <https://www.drugabuse.gov/publications/research-reports/cocaine/are-cocaine-abusers-risk-contracting-hiv-aids-hepatitis-b-c>
- National Institute on Drug Abuse. (2018a, January). The Matrix model (stimulants). <https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral-therapies/matrix>
- National Institute on Drug Abuse. (2018b, June). *Prescription stimulants DrugFacts*. <https://www.drugabuse.gov/publications/drugfacts/prescription-stimulants>
- National Institute on Drug Abuse. (2018c, July). The science of drug use and addiction: The basics. <https://www.drugabuse.gov/publications/media-guide/science-drug-use-addiction-basics>
- National Institute on Drug Abuse. (2019a). *Methamphetamine research report*. National Institutes of Health.
- National Institute on Drug Abuse. (2019b, October). How is methamphetamine different from other stimulants, such as cocaine? <https://www.drugabuse.gov/publications/research-reports/methamphetamine/how-methamphetamine-different-other-stimulants-such-cocaine>
- National Institute on Drug Abuse. (2019c, October). How is methamphetamine misused? <https://www.drugabuse.gov/publications/research-reports/methamphetamine/how-methamphetamine-misused>
- National Institute on Drug Abuse. (2019d, October). What is the scope of methamphetamine misuse in the United States? <https://www.drugabuse.gov/publications/research-reports/methamphetamine/what-scope-methamphetamine-misuse-in-united-states>
- National Institute on Drug Abuse. (2019e, October). What treatments are effective for people who misuse methamphetamine? <https://www.drugabuse.gov/publications/research-reports/methamphetamine/what-treatments-are-effective-people-who-misuse-methamphetamine>
- National Institute on Drug Abuse. (2019f, December 18). Monitoring the Future 2019 Survey results: Overall findings. <https://www.drugabuse.gov/drug-topics/trends-statistics/infographics/monitoring-future-2019-survey-results-overall-findings>
- National Institute on Drug Abuse. (2020a). *Drugs, brains, and behavior: The science of addiction* (NIH Publication No. 20-DA-5605). National Institutes of Health.
- National Institute on Drug Abuse. (2020b). *Misuse of prescription drugs research report*. National Institutes of Health.
- National Institute on Drug Abuse. (2020c, June). *Criminal justice DrugFacts*. National Institutes of Health. <https://www.drugabuse.gov/publications/drugfacts/criminal-justice>
- National Institute on Drug Abuse. (2021a, January 29). Overdose death rates. <https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates>
- National Institute on Drug Abuse. (2021b, March). *Cocaine DrugFacts*. <https://www.drugabuse.gov/publications/drugfacts/cocaine>
- Neeki, M. M., Dong, F., Liang, L., Toy, K., Carrico, B., Jabourian, N., ... Wong, D. (2018). Evaluation of the effect of methamphetamine on traumatic injury complications and outcomes. *Addiction Science and Clinical Practice*, 13(1), 11.



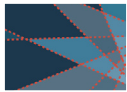
- Nelson, N. P., Weng, M. K., Hofmeister, M. G., Moore, K. L., Doshani, M., Kamili, S., ... Harris, A. M. (2020). Prevention of hepatitis A virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. *MMWR Recommendations and Reports*, 69(RR-5), 1–38.
- Nelson, P. K., Mathers, B. M., Cowie, B., Hagan, H., Des Jarlais, D., Horyniak, D., & Degenhardt, L. (2011). Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: Results of systematic reviews. *Lancet*, 378(9791), 571–583.
- Nerlander, L. M. C., Hoots, B. E., Bradley, H., Broz, D., Thorson, A., & Paz-Bailey, G. (2018). HIV infection among MSM who inject methamphetamine in 8 US cities. *Drug and Alcohol Dependence*, 190, 216–223.
- Newcomb, M. E., Ryan, D. T., Greene, G. J., Garofalo, R., & Mustanski, B. (2014). Prevalence and patterns of smoking, alcohol use, and illicit drug use in young men who have sex with men. *Drug and Alcohol Dependence*, 141, 65–71.
- Newton, T. F., De La Garza, R., Kalechstein, A. D., & Nestor, L. (2005). Cocaine and methamphetamine produce different patterns of subjective and cardiovascular effects. *Pharmacology, Biochemistry, and Behavior*, 82(1), 90–97.
- Nguyen, T. Q., Weir, B. W., Des Jarlais, D. C., Pinkerton, S. D., & Holtgrave, D. R. (2014). Syringe exchange in the United States: A national level economic evaluation of hypothetical increases in investment. *AIDS and Behavior*, 18(11), 2144–2155. doi:10.1007/s10461-014-0789-9
- Nickell, J. R., Siripurapu, K. B., Vartak, A., Crooks, P. A., & Dwoskin, L. P. (2014). The vesicular monoamine transporter-2: An important pharmacological target for the discovery of novel therapeutics to treat methamphetamine abuse. *Advances in Pharmacology*, 69, 71–106.
- NIDAnews [@NIDAnews]. (2014, September 11). "[Addiction] is like driving a car without brakes." – NIDA Director Dr. Nora Volkow at #TEDMED [Image attached] [Tweet]. Twitter. <https://twitter.com/nidanews/status/510086913160515584?lang=en>
- Niello, M., Gradisch, R., Loland, C. J., Stockner, T., & Sitte, H. H. (2020). Allosteric modulation of neurotransmitter transporters as a therapeutic strategy. *Trends in Pharmacological Sciences*, 41(7), 446–463.
- Nishino, S. (2009). Rebound hypersomnolence, stimulant abuse, and DAT-mediated dopamine release. *Sleep*, 32(11), 1407–1409.
- Nolan, S. O., Zachry, J. E., Johnson, A. R., Brady, L. J., Siciliano, C. A., & Calipari, E. S. (2020). Direct dopamine terminal regulation by local striatal microcircuitry. *Journal of Neurochemistry*, 155(5), 475–493.
- Norman, L., & Ford, J. (2018). Undergraduate prescription stimulant misuse: The impact of academic strain. *Substance Use and Misuse*, 53(9), 1482–1491.
- Novartis Pharmaceuticals. (2019). Ritalin and Ritalin-SR: Highlights of prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/010187s091,018029s059lbl.pdf
- Novick, T., Liu, Y., Alvanzo, A., Zonderman, A. B., Evans, M. K., & Crews, D. C. (2016). Lifetime cocaine and opiate use and chronic kidney disease. *American Journal of Nephrology*, 44(6), 447–453.
- Nowotny, K. M. (2015). Race/ethnic disparities in the utilization of treatment for drug dependent inmates in U.S. state correctional facilities. *Addictive Behaviors*, 40, 148–153.
- Nutt, D. J., Lingford-Hughes, A., Erritzoe, D., & Stokes, P. R. (2015). The dopamine theory of addiction: 40 years of highs and lows. *Nature Reviews Neuroscience*, 16(5), 305–312.
- Nuttbrock, L., Bockting, W., Rosenblum, A., Hwahng, S., Mason, M., Macri, M., & Becker, J. (2014). Gender abuse, depressive symptoms, and substance use among transgender women: A 3-year prospective study. *American Journal of Public Health*, 104(11), 2199–2206.
- Nyamathi, A., Hudson, A., Greengold, B., & Leake, B. (2012). Characteristics of homeless youth who use cocaine and methamphetamine. *American Journal on Addictions*, 121(3), 243–249.
- Nyamathi, A., Reback, C. J., Shoptaw, S., Salem, B. E., Zhang, S., & Yadav, K. (2017). Impact of tailored interventions to reduce drug use and sexual risk behaviors among homeless gay and bisexual men. *American Journal of Men's Health*, 11(2), 208–220.
- O'Brien, P., Crable, E., Fullerton, C., Hughley, L., & Truven Health Analytics. (2019). *Final project report: Best practices and barriers to engaging people with substance use disorders in treatment*. <https://aspe.hhs.gov/report/best-practices-and-barriers-engaging-people-substance-use-disorders-treatment>
- O'Connor, A., Harris, E., Hamilton, D., Fisher, C., & Sachmann, M. (2021). The experiences of pregnant women attending a specialist service and using methamphetamine. *Women and Birth*, 34(2), 170–179.
- O'Connor, E., Thomas, R., Senger, C. A., Perdue, L., Robalino, S., & Patnode, C. (2020). Interventions to prevent illicit and nonmedical drug use in children, adolescents, and young adults: Updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*, 323(20), 2067–2079.
- O'Donnell, J., Gladden, R. M., Mattson, C. L., Hunter, C. T., & Davis, N. L. (2020). Vital signs: Characteristics of drug overdose deaths involving opioids and stimulants—24 states and the District Columbia, January–June 2019. *Morbidity and Mortality Weekly Report*, 69(35), 1189–1197.

- Oei, J. L., Kingsbury, A., Dhawan, A., Burns, L., Feller, J. M., Clews, S., ... Abdel-Latif, M. E. (2012). Amphetamines, the pregnant woman, and her children: A review. *Journal of Perinatology*, 32(10), 737–747.
- O'Farrell, T. J., & Clements, K. (2012). Review of outcome research on marital and family therapy in treatment for alcoholism. *Journal of Marital and Family Therapy*, 38(1), 122–144.
- Office of Infectious Disease and HIV/AIDS Policy. (n.d.-a). Hepatitis B basic information. U.S. Department of Health and Human Services. <https://www.hhs.gov/hepatitis/learn-about-viral-hepatitis/hepatitis-b-basics/index.html>
- Office of Infectious Disease and HIV/AIDS Policy. (n.d.-b). Hepatitis C basic information. U.S. Department of Health and Human Services. <https://www.hhs.gov/hepatitis/learn-about-viral-hepatitis/hepatitis-c-basics/index.html#hcv-prevention>
- Office of the Surgeon General. (2016). *Facing addiction in America: The Surgeon General's report on alcohol, drugs, and health*. U.S. Department of Health and Human Services.
- Office of the Surgeon General. (2018, April 5). *U.S. Surgeon General's advisory on naloxone and opioid overdose*. <https://www.hhs.gov/surgeongeneral/priorities/opioids-and-addiction/naloxone-advisory/index.html>
- O'Halloran, C., Rice, B., White, E., Desai, M., Dunn, D. T., McCormack, S., ... Gafos, M. (2019). Chemsex is not a barrier to self-reported daily PrEP adherence among PROUD study participants. *International Journal on Drug Policy*, 74, 246–254.
- Ojikutu, B. O., Bogart, L. M., Higgins-Biddle, M., Dale, S. K., Allen, W., Dominique, T., & Mayer, K. H. (2018). Facilitators and barriers to pre-exposure prophylaxis (PrEP) use among Black individuals in the United States: Results from the National Survey on HIV in the Black Community (NSHBC). *AIDS and Behavior*, 22(11), 3576–3587.
- Otten, R., Mun, C. J., Shaw, D. S., Wilson, M. N., & Dishion, T. J. (2019). A developmental cascade model for early adolescent-onset substance use: The role of early childhood stress. *Addiction*, 114(2), 326–334.
- Overdose Response Strategy, New England High Intensity Drug Trafficking Area, & Boston Medical Center Office Based Addiction Treatment Training and Technical Assistance. (2020). *Methamphetamine: Public safety response*. Boston Medical Center Office Based Addiction Treatment Training and Technical Assistance.
- Pace, C. A., & Uebelacker, L. A. (2018). Addressing unhealthy substance use in primary care. *Medical Clinics of North America*, 102(4), 567–586.
- Page, K., Morris, M. D., Hahn, J. A., Maher, L., & Prins, M. (2013). Injection drug use and hepatitis C virus infection in young adult injectors: Using evidence to inform comprehensive prevention. *Clinical Infectious Diseases*, 57(Suppl. 2), S32–S38.
- Palamar, J. J., Davies, S., Ompad, D. C., Cleland, C. M., & Weitzman, M. (2015). Powder cocaine and crack use in the United States: An examination of risk for arrest and socioeconomic disparities in use. *Drug and Alcohol Dependence*, 149, 108–116.
- Pan, Y., Metsch, L. R., Wang, W., Philbin, M., Kyle, T. L., Gooden, L. K., & Feaster, D. J. (2020). The relationship between housing status and substance use and sexual risk behaviors among people currently seeking or receiving services in substance use disorder treatment programs. *Journal of Primary Prevention*, 41(4), 363–382.
- Paquette, C. E., Syvertsen, J. L., & Pollini, R. A. (2018). Stigma at every turn: Health services experiences among people who inject drugs. *International Journal of Drug Policy*, 57, 104–110.
- Paratz, E. D., Cunningham, N. J., & MacIsaac, A. I. (2016). The cardiac complications of methamphetamines. *Heart, Lung and Circulation*, 25(4), 325–332.
- Parsons, J. T., John, S. A., Millar, B. M., & Starks, T. J. (2018). Testing the efficacy of combined motivational interviewing and cognitive behavioral skills training to reduce methamphetamine use and improve HIV medication adherence among HIV-positive gay and bisexual men. *AIDS and Behavior*, 22(8), 2674–2686.
- Parvaz, M. A., Alia-Klein, N., Woicik, P. A., Volkow, N. D., & Goldstein, R. Z. (2011). Neuroimaging for drug addiction and related behaviors. *Reviews in the Neurosciences*, 22(6), 609–624.
- Patel, P., Borkowf, C. B., Brooks, J. T., Lasry, A., Lansky, A., & Mermin, J. (2014). Estimating per-act HIV transmission risk: A systematic review. *AIDS (London, England)*, 28(10), 1509–1519.
- Paterno, M. T., Fiddian-Green, A., & Gubrium, A. (2018). Moms supporting moms: Digital storytelling with peer mentors in recovery from substance use. *Health Promotion Practice*, 19(6), 823–832.
- Paulus, M. P., & Stewart, J. L. (2020). Neurobiology, clinical presentation, and treatment of methamphetamine use disorder. *JAMA Psychiatry*, 77(9), 959–966.
- PDR Network. (n.d.). Methylphenidate hydrochloride – drug summary. In *PDR: Prescribers' digital reference*. Retrieved March 8, 2021, from <https://www.pdr.net/drug-summary/Methylphenidate-Hydrochloride-ER-methylphenidate-hydrochloride-24298>
- Pedrelli, P., Nyer, M., Yeung, A., Zulauf, C., & Wilens, T. (2015). College students: Mental health problems and treatment considerations. *Academic Psychiatry*, 39(5), 503–511.
- Pendergraft, W. F., III, Herlitz, L. C., Thornley-Brown, D., Rosner, M., & Niles, J. L. (2014). Nephrotoxic effects of common and emerging drugs of abuse. *Clinical Journal of the American Society of Nephrology*, 9(11), 1996–2005.



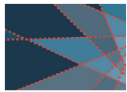
- Perry, C. J., & Lawrence, A. J. (2017). Addiction, cognitive decline and therapy: Seeking ways to escape a vicious cycle. *Genes, Brain and Behavior*, 16(1), 205–218.
- Perry, C. J., Zbukvic, I., Kim, J. H., & Lawrence, A. J. (2014). Role of cues and contexts on drug-seeking behaviour. *British Journal of Pharmacology*, 171(20), 4636–4672.
- Pescosolido, B. A., & Martin, J. K. (2015). The stigma complex. *Annual Review of Sociology*, 41(1), 87–116.
- Petit, A., Karila, L., Chalmin, F., & Lejoyeux, M. (2012). Methamphetamine addiction: A review of the literature. *Journal of Addiction Research and Therapy*, 51, 006. <https://www.omicsonline.org/methamphetamine-addiction-a-review-of-the-literature-2155-6105.S1-006.php?aid=3893>
- Petry, N. M. (2011). Contingency management: What it is and why psychiatrists should want to use it. *Psychiatrist*, 35(5), 161–163.
- Petry, N. M., Alessi, S. M., Barry, D., & Carroll, K. M. (2015). Standard magnitude prize reinforcers can be as efficacious as larger magnitude reinforcers in cocaine-dependent methadone patients. *Journal of Consulting and Clinical Psychology*, 83(3), 464–472.
- Pew Charitable Trusts. (2018). *More imprisonment does not reduce state drug problems*. <https://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2018/03/more-imprisonment-does-not-reduce-state-drug-problems>
- Pew Charitable Trusts. (2020). *Care coordination strategies for patients can improve substance use disorder outcomes* [Issue brief]. <https://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2020/04/care-coordination-strategies-for-patients-can-improve-substance-use-disorder-outcomes>
- Pew Research Center. (2020, May 6). Black imprisonment rate in the U.S. has fallen by a third since 2006. <https://www.pewresearch.org/fact-tank/2020/05/06/share-of-black-white-hispanic-americans-in-prison-2018-vs-2006/>
- Pham, T., Milanaik, R., Kaplan, A., Papaioannou, H., & Adesman, A. (2017). Household diversion of prescription stimulants: Medication misuse by parents of children with attention-deficit/hyperactivity disorder. *Journal of Child and Adolescent Psychopharmacology*, 27(8), 741–746.
- Philbin, M. M., Greene, E. R., Martins, S. S., LaBossier, N. J., & Mauro, P. M. (2020). Medical, nonmedical, and illegal stimulant use by sexual identity and gender. *American Journal of Preventive Medicine*, 59(5), 686–696.
- Philip, S. S., Yu, X., Donnell, D., Vittinghoff, E., & Buchbinder, S. (2010). Serosorting is associated with a decreased risk of HIV seroconversion in the EXPLORE study cohort. *PLoS One*, 5(9), e12662.
- Phillips, K. T. (2016). Barriers to practicing risk reduction strategies among people who inject drugs. *Addiction Research and Theory*, 24(1), 62–68.
- Pilgrim, J. L., Woodford, N., & Drummer, O. H. (2013). Cocaine in sudden and unexpected death: A review of 49 post-mortem cases. *Forensic Science International*, 227(1–3), 52–59.
- Pinedo, M., Zemore, S., & Rogers, S. (2018). Understanding barriers to specialty substance abuse treatment among Latinos. *Journal of Substance Abuse Treatment*, 94, 1–8.
- Piper, B. J., Ogden, C. L., Simoyan, O. M., Chung, D. Y., Caggiano, J. F., Nichols, S. D., & McCall, K. L. (2018). Trends in use of prescription stimulants in the United States and territories, 2006 to 2016. *PLoS One*, 13(11), e0206100.
- Plant, C. P., & Holland, J. M. (2018). Family behavior therapy for alcohol and drug problems in later-life. *Clinical Gerontologist*, 41(5), 508–515.
- Platt, L., Minozzi, S., Reed, J., Vickerman, P., Hagan, H., French, C., ... Hickman, M. (2017). Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.CD012021.pub2
- Polcin, D. L., Bond, J., Korcha, R., Nayak, M. B., Galloway, G. P., & Evans, K. (2014). Randomized trial of intensive motivational interviewing for methamphetamine dependence. *Journal of Addictive Diseases*, 33(3), 253–265.
- Polcin, D. L., Korcha, R., Bond, J., & Galloway, G. (2010). What did we learn from our study on sober living houses and where do we go from here? *Journal of Psychoactive Drugs*, 42(4), 425–433.
- Porcu, A., & Castelli, M. P. (2017). Cannabis and the use of amphetamine-like substances. In *Handbook of cannabis and related pathologies* (pp. e101–e110). Academic Press.
- Potenza, M. N., Balodis, I. M., Derevensky, J., Grant, J. E., Petry, N. M., Verdejo-Garcia, A., & Yip, S. W. (2019). Gambling disorder. *Nature Reviews Disease Primers*, 5(1), 51.
- Pradeep, T., & Standeven, L. R. (2019, January 3). Amphetamine. *Johns Hopkins Psychiatry Guide*. https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_Psychiatry_Guide/787274/all/Amphetamine
- Preston, K. L., Schroeder, J. R., Kowalczyk, W. J., Phillips, K. A., Jobes, M. L., Dwyer, M., ... Epstein, D. H. (2018). End-of-day reports of daily hassles and stress in men and women with opioid-use disorder: Relationship to momentary reports of opioid and cocaine use and stress. *Drug and Alcohol Dependence*, 193, 21–28.
- Priester, M. A., Browne, T., Iachini, A., Clone, S., DeHart, D., & Seay, K. D. (2016). Treatment access barriers and disparities among individuals with co-occurring mental health and substance use disorders: An integrative literature review. *Journal of Substance Abuse Treatment*, 61, 47–59.

- Prochaska, J. O., DiClemente, C. C., & Norcross, J. C. (1992). In search of how people change: Applications to addictive behaviors. *American Psychologist*, 47(9), 1102–1114.
- Proctor, S. L., Hoffmann, N. G., & Raggio, A. (2019). Prevalence of substance use disorders and psychiatric conditions among county jail inmates: Changes and stability over time. *Criminal Justice and Behavior*, 46(1), 24–41.
- Qiao, S., Zhou, G., & Li, X. (2018). Disclosure of same-sex behaviors to health-care providers and uptake of HIV testing for men who have sex with men: A systematic review. *American Journal of Men's Health*, 12(5), 1197–1214.
- Quednow, B. B., & Vonmoos, M. (2017). Cognitive dysfunctions in chronic cocaine users. In V. R. Preedy (Ed.), *The neuroscience of cocaine: Mechanisms and treatment* (pp. 395–405). Academic Press.
- Quinn, P. D., Chang, Z., Hur, K., Gibbons, R. D., Lahey, B. B., Rickert, M. E., ... D'Onofrio, B. M. (2017). ADHD medication and substance-related problems. *American Journal of Psychiatry*, 174(9), 877–885.
- Rabiner, D. L. (2013). Stimulant prescription cautions: Addressing misuse, diversion and malingering. *Current Psychiatry Reports*, 15(7), 375.
- Radfar, S. R., & Rawson, R. A. (2014). Current research on methamphetamine: Epidemiology, medical and psychiatric effects, treatment, and harm reduction efforts. *Addiction and Health*, 6(3–4), 146–154.
- Raiker, N., Aouthmany, M., & Ezra, N. (2016). Dermatologic signs and symptoms of substance abuse. *Journal of Clinical and Experimental Dermatology Research*, 7(2), 337.
- Ramesh, D., Keyser-Marcus, L. A., Ma, L., Schmitz, J. M., Lane, S. D., Marwitz, J. H., ... Moeller, F. G. (2015). Prevalence of traumatic brain injury in cocaine-dependent research volunteers. *American Journal on Addictions*, 24(4), 341–347.
- Ramirez, R. L., III, Perez, V. D. J., & Zamanian, R. T. (2018a). Methamphetamine and the risk of pulmonary arterial hypertension. *Current Opinion in Pulmonary Medicine*, 24(5), 416–424.
- Ramirez, R. L., III, Perez, V. D. J., & Zamanian, R. T. (2018b). Stimulants and pulmonary arterial hypertension: An update. *Advances in Pulmonary Hypertension*, 17(2), 49–54.
- Ramsey, A. T., Satterfield, J. M., Gerke, D. R., & Proctor, E. K. (2019). Technology-based alcohol interventions in primary care: Systematic review. *Journal of Medical Internet Research*, 21(4), e10859.
- Rash, C. J., Alessi, S. M., & Petry, N. M. (2017). Substance abuse treatment patients in housing programs respond to contingency management interventions. *Journal of Substance Abuse Treatment*, 72, 97–102.
- Rash, C. J., Burki, M., Montezuma-Rusca, J. M., & Petry, N. M. (2016). A retrospective and prospective analysis of trading sex for drugs or money in women substance abuse treatment patients. *Drug and Alcohol Dependence*, 162, 182–189.
- Ratcliffe, M., Burd, C., Holder, K., & Fields, A. (2016). *Defining rural at the U.S. Census Bureau (ACSGEO-1)*. U.S. Census Bureau.
- Rawson, R. A. (2010). Treatments for methamphetamine dependence: Contingency management and the Matrix model. In R. Pates & D. Riley (Eds.), *Interventions for amphetamine misuse* (pp. 83–100). Wiley-Blackwell.
- Rawson, R. A. (2013). Current research on the epidemiology, medical and psychiatric effects, and treatment of methamphetamine use. *Journal of Food and Drug Analysis*, 21(4), S77–S81.
- Rawson, R. (2020). *Stimulant use by patients on medication for opioid use disorder: Do we have any answers?* [PowerPoint slides]. https://uclaisap.org/ntpreach/docs/RR-Meth-and-MOUD_05-01-20.pdf
- Rawson, R. A., Chudzynski, J., Gonzales, R., Mooney, L., Dickerson, D., Ang, A., ... Cooper, C. B. (2015). The impact of exercise on depression and anxiety symptoms among abstinent methamphetamine-dependent individuals in a residential treatment setting. *Journal of Substance Abuse Treatment*, 57, 36–40.
- Rawson, R. A., Chudzynski, J., Mooney, L., Gonzales, R., Ang, A., Dickerson, D., ... Cooper, C. B. (2015). Impact of an exercise intervention on methamphetamine use outcomes post-residential treatment care. *Drug and Alcohol Dependence*, 156, 21–28.
- Rawson, R. A., Gonzales, R., & Brethen, P. (2002). Treatment of methamphetamine use disorders: An update. *Journal of Substance Abuse Treatment*, 23(2), 145–150.
- Rawson, R. A., Huber, A., Brethen, P., Shoptaw, S., & Ling, W. (1996). *Methamphetamine and cocaine: Comparison of reported effects and response to treatment* [Paper presentation]. CPDD Satellite Conference on Methamphetamine, San Juan, Puerto Rico, United States.
- Rawson, R. A., Ling, W., & Mooney, L. J. (2015). Clinical management: Methamphetamine. In M. Galanter, H. D. Kleber, & K. T. Brady (Eds.), *Textbook of substance abuse treatment* (5th ed., chapter 14). American Psychiatric Association Publishing.
- Rawson, R. A., Obert, J. L., McCann, M. J., & Ling, W. (1991). *The Matrix model of outpatient treatment for alcohol use and dependency*. The Matrix Center.



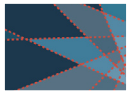
- Rawson, R. A., Obert, J. L., McCann, M. J., & Ling, W. (1993). Neurobehavioral treatment for cocaine dependency: A preliminary evaluation. In F. M. Tims & C. G. Leukefeld (Eds.), *Cocaine treatment: Research and clinical perspectives* (pp. 92–115). NIDA Research Monograph Series, Number 135, DHHS Publication No. (ADM) 93-3639. National Institute on Drug Abuse.
- Rawson, R. A., Schmidt, K., & Mooney, L. J. (2021). Treatment of stimulant-related disorders. In K. T. Brady, F. R. Levin, M. Galanter, & H. D. Kleber (Eds.), *The American Psychiatric Association Publishing textbook of substance use disorder treatment* (6th ed., pp. 161–178). American Psychiatric Association Publishing.
- Ray, L. A., Bujarski, S., Courtney, K. E., Moallem, N. R., Lunny, K., Roche, D., ... Miotto, K. (2015). The effects of naltrexone on subjective response to methamphetamine in a clinical sample: A double-blind, placebo-controlled laboratory study. *Neuropsychopharmacology*, 40(10), 2347–2356.
- Reddy, P., Ng, T., Oh, E. E., Moady, G., & Elkayam, U. (2020). Clinical characteristics and management of methamphetamine-associated cardiomyopathy: State-of-the-art review. *Journal of the American Heart Association*, 9(11), e016704.
- Regier, P. S., & Redish, A. D. (2015). Contingency management and deliberative decision-making processes. *Frontiers in Psychiatry*, 6, 76.
- Reif, S., Braude, L., Lyman, D. R., Dougherty, R. H., Daniels, A. S., Ghose, S. S., ... Delphin-Rittmon, M. E. (2014). Peer recovery support for individuals with substance use disorders: Assessing the evidence. *Psychiatric Services*, 65(7), 853–861.
- Restrepo, C. S., Carrillo, J. A., Martínez, S., Ojeda, P., Rivera, A. L., & Hattar, A. (2007). Pulmonary complications from cocaine and cocaine-based substances: Imaging manifestations. *RadioGraphics*, 27(4), 941–956.
- Rhoades, H., Winetrobe, H., & Rice, E. (2014). Prescription drug misuse among homeless youth. *Drug and Alcohol Dependence*, 138, 229–233.
- Richard, J., Potenza, M. N., Ivoska, W., & Derevensky, J. (2019). The stimulating nature of gambling behaviors: Relationships between stimulant use and gambling among adolescents. *Journal of Gambling Studies*, 35(1), 47–62.
- Richards, J. R., Garber, D., Laurin, E. G., Albertson, T. E., Derlet, R. W., Amsterdam, E. A., ... Lange, R. A. (2016). Treatment of cocaine cardiovascular toxicity: A systematic review. *Clinical Toxicology*, 54(5), 345–364.
- Richards, J. R., Hamidi, S., Grant, C. D., Wang, C. G., Tabish, N., Turnipseed, S. D., & Derlet, R. W. (2017). Methamphetamine Use and emergency department utilization: 20 years later. *Journal of Addiction*, 2017, 4050932.
- Richards, J. R., Hawkins, J. A., Acevedo, E. W., & Laurin, E. G. (2019). The care of patients using methamphetamine in the emergency department: Perception of nurses, residents, and faculty. *Substance Abuse*, 40(1), 95–101.
- Richards, J. R., & Laurin, E. G. (2020). Methamphetamine toxicity. In *StatPearls*. Retrieved March 19, 2021, from <https://www.ncbi.nlm.nih.gov/books/NBK430895/>
- Richards, J. R., & Le, J. K. (2020). Cocaine toxicity. In *StatPearls*. Retrieved March 19, 2021, from <https://www.ncbi.nlm.nih.gov/books/NBK430976/>
- Richards, J. R., Mefford, J. M., Patel, J. J., Parikh, A. K., Eder, A. Z., & Elder, J. W. (2020). The association between cocaine use detected on drug screening and rhabdomyolysis. *Toxicology Communications*, 4(1), 18–24.
- Richards, J. R., Wang, C. G., Fontenette, R. W., Stuart, R. P., McMahon, K. F., & Turnipseed, S. D. (2020). Rhabdomyolysis, methamphetamine, amphetamine and MDMA use: Associated factors and risks. *Journal of Dual Diagnosis*, 16(4), 429–437.
- Rieckmann, T., Moore, L. A., Croy, C. D., Novins, D. K., & Aarons, G. (2016). A national study of American Indian and Alaska Native substance abuse treatment: Provider and program characteristics. *Journal of Substance Abuse Treatment*, 68, 46–56.
- Riley, E. D., Evans, J. L., Hahn, J. A., Briceno, A., Davidson, P. J., Lum, P. J., & Page, K. (2016). A longitudinal study of multiple drug use and overdose among young people who inject drugs. *American Journal of Public Health*, 106(5), 915–917.
- Ritchwood, T. D., DeCoster, J., Metzger, I. W., Bolland, J. M., & Danielson, C. K. (2016). Does it really matter which drug you choose? An examination of the influence of type of drug on type of risky sexual behavior. *Addictive Behaviors*, 60, 97–102.
- Ritchwood, T. D., Ford, H., DeCoster, J., Sutton, M., & Lochman, J. E. (2015). Risky sexual behavior and substance use among adolescents: A meta-analysis. *Children and Youth Services Review*, 52, 74–88.
- Rivera, A. V., DeCuir, J., Crawford, N. D., Amesty, S., & Lewis, C. F. (2014). Internalized stigma and sterile syringe use among people who inject drugs in New York City, 2010–2012. *Drug and Alcohol Dependence*, 144, 259–264.
- Robbins, J. L., Wenger, L., Lorrivick, J., Shiboski, C., & Kral, A. H. (2010). Health and oral health care needs and health care-seeking behavior among homeless injection drug users in San Francisco. *Journal of Urban Health*, 87(6), 920–930.
- Robertson, C. L., Ishibashi, K., Chudzynski, J., Mooney, L. J., Rawson, R. A., Dolezal, B. A., ... London, E. D. (2016). Effect of exercise training on striatal dopamine D2/D3 receptors in methamphetamine users during behavioral treatment. *Neuropsychopharmacology*, 41(6), 1629–1636.

- Robertson, E. B., Sims, B. E., & Reider, E. E. (2016). Risk and protective factors. In E. Wargo (Ed.), *Principles of substance abuse prevention for early childhood: A research-based guide* (pp. 21–32). National Institutes of Health, National Institute on Drug Abuse.
- Roche, D. J. O., Worley, M. J., Courtney, K. E., Bujarski, S., London, E. D., Shoptaw, S., & Ray, L. A. (2017). Naltrexone moderates the relationship between cue-induced craving and subjective response to methamphetamine in individuals with methamphetamine use disorder. *Psychopharmacology*, 234(13), 1997–2007.
- Rolland, B., Karila, L., Geoffroy, P. A., & Cottencin, O. (2011). Shared vulnerability between seizures and psychosis in cocaine addiction? *Epilepsy and Behavior*, 22(3), 596–598.
- Ronsley, C., Nolan, S., Knight, R., Hayashi, K., Klimas, J., Walley, A., ... Fairbairn, N. (2020). Treatment of stimulant use disorder: A systematic review of reviews. *PLoS One*, 15(6), e0234809.
- Ropelewski, L. R., Mancha, B. E., Hulbert, A., Rudolph, A. E., & Martins, S. S. (2011). Correlates of risky injection practices among past-year injection drug users among the US general population. *Drug and Alcohol Dependence*, 116(1–3), 64–71.
- Rosino, M., & Hughey, M. (2018). The war on drugs, racial meanings, and structural racism: A holistic and reproductive approach. *American Journal of Economics and Sociology*, 77, 849–892.
- Rowe, C., Santos, G. M., McFarland, W., & Wilson, E. C. (2015). Prevalence and correlates of substance use among trans female youth ages 16–24 years in the San Francisco Bay Area. *Drug and Alcohol Dependence*, 147, 160–166.
- Ruglass, L. M., Hien, D. A., Hu, M. C., & Campbell, A. N. (2014). Associations between post-traumatic stress symptoms, stimulant use, and treatment outcomes: A secondary analysis of NIDA's Women and Trauma Study. *American Journal on Addictions*, 23(1), 90–95.
- Ruglass, L. M., Shevorykin, A., Brezing, C., Hu, M.-C., & Hien, D. A. (2017). Demographic and clinical characteristics of treatment seeking women with full and subthreshold PTSD and concurrent cannabis and cocaine use disorders. *Journal of Substance Abuse Treatment*, 80, 45–51.
- Rutter, L. A., & Brown, T. A. (2017). Psychometric properties of the Generalized Anxiety Disorder Scale-7 (GAD-7) in outpatients with anxiety and mood disorders. *Journal of Psychopathology and Behavioral Assessment*, 39(1), 140–146.
- Ryan, S. A. (2019). Cocaine use in adolescents and young adults. *Pediatric Clinics of North America*, 66(6), 1135–1147.
- Sahker, E., Ali, S. R., & Arndt, S. (2019). Employment recovery capital in the treatment of substance use disorders: Six-month follow-up observations. *Drug and Alcohol Dependence*, 205, 107624.
- Sahker, E., Yeung, C. W., Garrison, Y. L., Park, S., & Arndt, S. (2017). Asian American and Pacific Islander substance use treatment admission trends. *Drug and Alcohol Dependence*, 171, 1–8.
- Saitz, R., Bair-Merritt, M. H., & Levy, S. J. (2021). Screening for young adults for illicit drug use: A good idea although evidence is lacking. *Pediatrics*, 147(Suppl. 2), S259–S261.
- Saitz, R., Cheng, D. M., Allensworth-Davies, D., Winter, M. R., & Smith, P. C. (2014). The ability of single screening questions for unhealthy alcohol and other drug use to identify substance dependence in primary care. *Journal of Studies on Alcohol and Drugs*, 75(1), 153–157.
- Salamanca, S. A., Sorrentino, E. E., Nosanchuk, J. D., & Martinez, L. R. (2015). Impact of methamphetamine on infection and immunity. *Frontiers in Neuroscience*, 8, 445.
- Salas-Wright, C. P., Lee, S., Vaughn, M. G., Jang, Y., & Sanglang, C. C. (2015). Acculturative heterogeneity among Asian/Pacific Islanders in the United States: Associations with DSM mental and substance use disorders. *American Journal of Orthopsychiatry*, 85(4), 362–370.
- Saldana, C. S., Vyas, D. A., & Wurcel, A. G. (2020). Soft tissue, bone, and joint infections in people who inject drugs. *Infectious Disease Clinics of North America*, 34(3), 495–509.
- Salloum, I. M., & Brown, E. S. (2017). Management of comorbid bipolar disorder and substance use disorders. *American Journal of Drug and Alcohol Abuse*, 43(4), 366–376.
- Salmanzadeh, H., Ahmadi-Soleimani, S. M., Pachenari, N., Azadi, M., Halliwell, R. F., Rubino, T., & Azizi, H. (2020). Adolescent drug exposure: A review of evidence for the development of persistent changes in brain function. *Brain Research Bulletin*, 156, 105–117.
- Salo, R., Flower, K., Kielstein, A., Leamon, M. H., Nordahl, T. E., & Galloway, G. P. (2011). Psychiatric comorbidity in methamphetamine dependence. *Psychiatry Research*, 186(2–3), 356–361.
- Saloner, B., Bandara, S. N., McGinty, E. E., & Barry, C. L. (2016). Justice-involved adults with substance use disorders: Coverage increased but rates of treatment did not in 2014. *Health Affairs (Millwood)*, 35(6), 1058–1066.
- Samuels, E. A., Baird, J., Yang, E. S., & Mello, M. J. (2019). Adoption and utilization of an emergency department naloxone distribution and peer recovery coach consultation program. *Academic Emergency Medicine*, 26(2), 160–173.



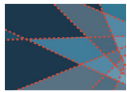
- Sanchez, K., Chartier, K. G., Greer, T. L., Walker, R., Carmody, T., Rethorst, C. D., ... Trivedi, M. H. (2015). Comorbidities and race/ethnicity among adults with stimulant use disorders in residential treatment. *Journal of Ethnicity in Substance Abuse, 14*(1), 79–95.
- Sanchez, K., Greer, T. L., Walker, R., Carmody, T., Rethorst, C. D., & Trivedi, M. H. (2017). Racial and ethnic differences in treatment outcomes among adults with stimulant use disorders after a dosed exercise intervention. *Journal of Ethnicity in Substance Abuse, 16*(4), 495–510.
- Sánchez-Hervás, E., & Llorente del Pozo, J. M. (2012). Recaídas en la adicción a cocaína: Una revisión [Relapse in cocaine addiction: A review]. *Adicciones, 24*(3), 269–279.
- Sanders, M. (2011). Strategies for engaging difficult-to-reach, multiproblem clients with substance use disorders. *Alcoholism Treatment Quarterly, 29*(1), 91–98.
- Sanders, M. (2015). *Counseling African Americans with substance use disorders*. [Handout showing PowerPoint slides]. https://www.naadac.org/assets/2416/2015-06-04_counseling_african_americans_with_suds_webinarslides.pdf
- Sanner, L. M., & Greene, M. S. (2020). *Social determinants of health and their impact on mental health and substance misuse*. Center for Health Policy at the Indiana University School of Public Health.
- Santoro, P., Rodríguez, R., Morales, P., Morano, A., & Morán, M. (2020). One “chemsex” or many? Types of chemsex sessions among gay and other men who have sex with men in Madrid, Spain: Findings from a qualitative study. *International Journal of Drug Policy, 82*, 102790.
- Saunders, E. C., Lambert-Harris, C., McGovern, M. P., Meier, A., & Xie, H. (2015). The prevalence of posttraumatic stress disorder symptoms among addiction treatment patients with cocaine use disorders. *Journal of Psychoactive Drugs, 47*(1), 42–50.
- Sayegh, C. S., Huey, S. J., Jr., Zara, E. J., & Jhaveri, K. (2017). Follow-up treatment effects of contingency management and motivational interviewing on substance use: A meta-analysis. *Psychology of Addictive Behaviors, 31*(4), 403–414.
- Scheim, A. I., Bauer, G. R., & Shokoohi, M. (2017). Drug use among transgender people in Ontario, Canada: Disparities and associations with social exclusion. *Addictive Behaviors, 72*, 151–158.
- Schierenberg, A., van Amsterdam, J., van den Brink, W., & Goudriaan, A. E. (2012). Efficacy of contingency management for cocaine dependence treatment: A review of the evidence. *Current Drug Abuse Reviews, 5*(4), 320–331.
- Schillie, S., Vellozzi, C., Reingold, A., Harris, A., Haber, P., Ward, J. W., & Nelson, N. P. (2018). Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Recommendations and Reports, 67*(RR-1), 1–31.
- Schneider, J. A., Cornwell, B., Ostrow, D., Michaels, S., Schumm, P., Laumann, E. O., & Friedman, S. (2013). Network mixing and network influences most linked to HIV infection and risk behavior in the HIV epidemic among black men who have sex with men. *American Journal of Public Health, 103*(1), e28–e36.
- Schottenfeld, R. S., Chawarski, M. C., Cubells, J. F., George, T. P., Lappalainen, J., & Kosten, T. R. (2014). Randomized clinical trial of disulfiram for cocaine dependence or abuse during buprenorphine treatment. *Drug and Alcohol Dependence, 136*, 36–42.
- Schottenfeld, R. S., Moore, B., & Pantalon, M. V. (2011). Contingency management with community reinforcement approach or twelve-step facilitation drug counseling for cocaine dependent pregnant women or women with young children. *Drug and Alcohol Dependence, 118*(1), 48–55.
- Schumm, J. A., & Gore, W. L. (2016). Simultaneous treatment of co-occurring posttraumatic stress disorder and substance use disorder. *Current Treatment Options in Psychiatry, 3*(1), 28–36.
- Scoglio, A. A., Gorman, J. A., Park, D., Jooma, S., & Kraus, S. W. (2020). Trauma-informed drug screens for veterans with co-occurring disorders: A case series. *Journal of Dual Diagnosis, 16*(3), 347–356.
- Searight, R. (2018). Counseling patients in primary care: Evidence-based strategies. *American Family Physician, 98*, 719–728.
- See, I., Gokhale, R. H., Geller, A., Lovegrove, M., Schranz, A., Fleischauer, A., ... Fiore, A. (2020). National public health burden estimates of endocarditis and skin and soft-tissue infections related to injection drug use: A review. *Journal of Infectious Diseases, 222*(Suppl. 5), S429–S436.
- Sembower, M. A., Ertischek, M. D., Buchholtz, C., Dasgupta, N., & Schnoll, S. H. (2013). Surveillance of diversion and nonmedical use of extended-release prescription amphetamine and oral methylphenidate in the United States. *Journal of Addictive Diseases, 32*(1), 26–38.
- Semple, S. J., Strathdee, S. A., Zians, J., McQuaid, J. R., & Patterson, T. L. (2011). Drug assertiveness and sexual risk-taking behavior in a sample of HIV-positive, methamphetamine-using men who have sex with men. *Journal of Substance Abuse Treatment, 41*(3), 265–272.
- Sevelius, J. M., Patouhas, E., Keatley, J. G., & Johnson, M. O. (2014). Barriers and facilitators to engagement and retention in care among transgender women living with human immunodeficiency virus. *Annals of Behavioral Medicine, 47*(1), 5–16.
- Servtson, S. G., Kreider, S. E. D., Olsen, H., Ellis, M. S., Cicero, T. J., & Dart, R. C. (2019). RADARS System Quarterly Technical Report: *The prevalence of methamphetamine use is increasing among individuals entering medication-assisted treatment programs for opioid use disorders (2019–Q3)*. RADARS System.

- Sewell, J., Cambiano, V., Miltz, A., Speakman, A., Lampe, F. C., Phillips, A., ... Rodger, A. (2018). Changes in recreational drug use, drug use associated with chemsex, and HIV-related behaviours, among HIV-negative men who have sex with men in London and Brighton, 2013–2016. *Sexually Transmitted Infections*, 94(7), 494–501.
- Sewell, J., Miltz, A., Lampe, F. C., Cambiano, V., Speakman, A., Phillips, A. N., ... Rodger, A. J. (2017). Poly drug use, chemsex drug use, and associations with sexual risk behaviour in HIV-negative men who have sex with men attending sexual health clinics. *International Journal of Drug Policy*, 43, 33–43.
- Shahrokh, N. C., Hales, R. E., Phillips, K. A., & Yudofsky, S. C. (2011). *The language of mental health: A glossary of psychiatric terms*. American Psychiatric Publishing.
- Sharma, A., & Stan, M. N. (2019). Thyrotoxicosis: Diagnosis and management. *Mayo Clinic Proceedings*, 94(6), 1048–1064.
- Sharma, T., Kumar, M., Rizkallah, A., Cappelluti, E., & Padmanabhan, P. (2019). Cocaine-induced thrombosis: Review of predisposing factors, potential mechanisms, and clinical consequences with a striking case report. *Cureus*, 11(5), e4700.
- Shearer, R. D., Howell, B. A., Bart, G., & Winkelman, T. N. A. (2020). Substance use patterns and health profiles among US adults who use opioids, methamphetamine, or both, 2015–2018. *Drug and Alcohol Dependence*, 214, 108162.
- Shekarchizadeh, H., Khami, M. R., Mohebbi, S. Z., Ekhtiari, H., & Virtanen, J. I. (2013). Oral health of drug abusers: A review of health effects and care. *Iranian Journal of Public Health*, 42(9), 929–940.
- Shen, W. W., Zhang, Y. S., Li, L. H., Liu, Y., Huang, X. N., Chen, L. H., & Zhou, W. (2014). Long-term use of methamphetamine disrupts the menstrual cycles and hypothalamic-pituitary-ovarian axis. *Journal of Addiction Medicine*, 8(3), 183–188.
- Sherman, C. (2017, March 9). Impacts of drugs on neurotransmission. National Institute on Drug Abuse. <https://www.drugabuse.gov/news-events/nida-notes/2017/03/impacts-drugs-neurotransmission>
- Shetty, V., Harrell, L., Clague, J., Murphy, D. A., Dye, B. A., & Belin, T. R. (2016). Methamphetamine users have increased dental disease: A propensity score analysis. *Journal of Dental Research*, 95(7), 814–821.
- Shetty, V., Harrell, L., Murphy, D. A., Vitero, S., Gutierrez, A., Belin, T. R., ... Spolsky, V. W. (2015). Dental disease patterns in methamphetamine users: Findings in a large urban sample. *Journal of the American Dental Association* (1939), 146(12), 875–885.
- Shetty, V., Mooney, L. J., Zigler, C. M., Belin, T. R., Murphy, D., & Rawson, R. (2010). The relationship between methamphetamine use and increased dental disease. *Journal of the American Dental Association* (1939), 141(3), 307–318.
- Shin, E. J., Dang, D. K., Tran, T. V., Tran, H. Q., Jeong, J. H., Nah, S. Y., ... Kim, H. C. (2017). Current understanding of methamphetamine-associated dopaminergic neurodegeneration and psychotoxic behaviors. *Archives of Pharmacol Research*, 40(4), 403–428.
- Shoptaw, S., Rawson, R. A., McCabb, M. J., & Obert, J. L. (1994). The Matrix model of outpatient stimulant abuse treatment: Evidence of efficacy. *Journal of Addictive Diseases*, 13(4), 129–141.
- Siciliano, C. A., Calipari, E. S., Ferris, M. J., & Jones, S. R. (2015). Adaptations of presynaptic dopamine terminals induced by psychostimulant self-administration. *ACS Chemical Neuroscience*, 6(1), 27–36.
- Silvers, J. A., Squeglia, L. M., Rømer Thomsen, K., Hudson, K. A., & Feldstein Ewing, S. W. (2019). Hunting for what works: Adolescents in addiction treatment. *Alcoholism: Clinical and Experimental Research*, 43(4), 578–592.
- Simon, D. P., & Kreek, M. J. (2016). Cocaine: Usage, misuse, and addiction processes—An overview. In V. Preedy (Ed.), *Neuropathology of drug addictions and substance misuse* (Vol. 2, pp. 5–13). Elsevier.
- Sinha, R. (2013). The clinical neurobiology of drug craving. *Current Opinion in Neurobiology*, 23(4), 649–654.
- Sisson, R., & Azrin, N. H. (1989). The community reinforcement approach. In R. K. Hester & W. R. Miller (Eds.), *Handbook of alcoholism treatment approaches: Effective alternatives* (Vol. 157, pp. 242–258). Pergamon Press.
- Skewes, M. C., & González, V. M. (2013). The biopsychosocial model of addiction. In P. M. Miller (Ed.), *Principles of addiction: Comprehensive addiction behaviors and disorders* (Vol. 1, pp. 61–70). Elsevier.
- Slesnick, N., & Zhang, J. (2016). Family systems therapy for substance-using mothers and their 8- to 16-year-old children. *Psychology of Addictive Behaviors*, 30(6), 619–629.
- Smid, M. C., Metz, T. D., & Gordon, A. J. (2019). Stimulant use in pregnancy: An under-recognized epidemic among pregnant women. *Clinical Obstetrics and Gynecology*, 62(1), 168–184.
- Smith, L. M., Diaz, S., Lagasse, L. L., Woudes, T., Derauf, C., Newman, E., ... Lester, B. M. (2015). Developmental and behavioral consequences of prenatal methamphetamine exposure: A review of the Infant Development, Environment, and Lifestyle (IDEAL) Study. *Neurotoxicology and Teratology*, 51, 35–44.
- Smith, M. A., & Witte, M. A. (2012). The effects of exercise on cocaine self-administration, food-maintained responding, and locomotor activity in female rats: Importance of the temporal relationship between physical activity and initial drug exposure. *Experimental and Clinical Psychopharmacology*, 20(6), 437–446.



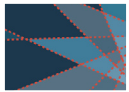
- Smith, P. H., Homish, G. G., Leonard, K. E., & Cornelius, J. R. (2012). Intimate partner violence and specific substance use disorders: Findings from the National Epidemiologic Survey on Alcohol and Related Conditions. *Psychology of Addictive Behaviors*, 26(2), 236–245.
- Smith, V., & Tasker, F. (2017). Gay men's chemsex survival stories. *Sexual Health*, 15(2), 116–122.
- Smullin, C., Wagman, J., Mehta, S., & Klausner, J. D. (2021). A narrative review of the epidemiology of congenital syphilis in the United States from 1980 to 2019. *Sexually Transmitted Diseases*, 48(2), 71–78.
- Solingapuram Sai, J., Hurley, R. A., Dodda, M., & Taber, K. H. (2019). Positron emission tomography: Updates on imaging of addiction. *Journal of Neuropsychiatry and Clinical Neurosciences*, 31(4), A6–A288.
- Soontornniyomkij, V., Kesby, J. P., Morgan, E. E., Bischoff-Grethe, A., Minassian, A., Brown, G. G., ... Translational Methamphetamine AIDS Research Center (TMARC) Group. (2016). Effects of HIV and methamphetamine on brain and behavior: Evidence from human studies and animal models. *Journal of Neuroimmune Pharmacology*, 11(3), 495–510.
- Spillane, N. S., Weyandt, L., Oster, D., & Treloar, H. (2017). Social contextual risk factors for stimulant use among adolescent American Indians. *Drug and Alcohol Dependence*, 179, 167–173.
- Spiller, H. A., Hays, H. L., & Aleguas, A. (2013). Overdose of drugs for attention-deficit hyperactivity disorder: Clinical presentation, mechanisms of toxicity, and management. *CNS Drugs*, 27(7), 531–543.
- Spronk, D. B., van Wel, J. H. P., Ramaekers, J. G., & Verkes, R. J. (2013). Characterizing the cognitive effects of cocaine: A comprehensive review. *Neuroscience and Biobehavioral Reviews*, 37(8), 1838–1859.
- Staiger, P. K., Richardson, B., Long, C. M., Carr, V., & Marlatt, G. A. (2013). Overlooked and underestimated? Problematic alcohol use in clients recovering from drug dependence. *Addiction*, 108(7), 1188–1193.
- Stanger, C., & Budney, A. J. (2019). Contingency management: Using incentives to improve outcomes for adolescent substance use disorders. *Pediatric Clinics of North America*, 66(6), 1183–1192.
- Stanger, C., & Noel, V. (2014). A social skills and parental training intervention for disruptive boys reduces substance use behaviours in adolescence. *Evidence-Based Mental Health*, 17(1), 23.
- Steingard, R., Taskiran, S., Connor, D. F., Markowitz, J. S., & Stein, M. A. (2019). New formulations of stimulants: An update for clinicians. *Journal of Child and Adolescent Psychopharmacology*, 29(5), 324–339.
- Stevens, O., Moncrieff, M., & Gafos, M. (2020). Chemsex-related drug use and its association with health outcomes in men who have sex with men: A cross-sectional analysis of Antidote clinic service data. *Sexually Transmitted Infections*, 96(2), 124–130.
- Stitzer, M. L., Gukasyan, N., Matheson, T., Sorensen, J. L., Feaster, D. J., Duan, R., ... Metsch, L. R. (2020). Enhancing patient navigation with contingent financial incentives for substance use abatement in persons with HIV and substance use. *Psychology of Addictive Behaviors*, 34(1), 23–30.
- Stoddard, S. A., Epstein-Ngo, Q., Walton, M. A., Zimmerman, M. A., Chermack, S. T., Blow, F. C., ... Cunningham, R. M. (2015). Substance use and violence among youth: A daily calendar analysis. *Substance Use and Misuse*, 50(3), 328–339.
- Stoicescu, C., Ameilia, R., Irwanto, Praptoraharjo, I., & Mahanani, M. (2019). Syndemic and synergistic effects of intimate partner violence, crystal methamphetamine, and depression on HIV sexual risk behaviors among women who inject drugs in Indonesia. *Journal of Urban Health*, 96(3), 477–496.
- Stoops, W. W., & Rush, C. R. (2013). Agonist replacement for stimulant dependence: A review of clinical research. *Current Pharmaceutical Design*, 19(40), 7026–7035.
- Storebø, O. J., Ramstad, E., Krogh, H. B., Nilausen, T. D., Skoog, M., Holmskov, M., ... Gluud, C. (2015). Methylphenidate for children and adolescents with attention deficit hyperactivity disorder (ADHD). *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.CD009885.pub2
- Strickland, J. C., Havens, J. R., & Stoops, W. W. (2019). A nationally representative analysis of “twin epidemics”: Rising rates of methamphetamine use among persons who use opioids. *Drug and Alcohol Dependence*, 204, 107592.
- Stringfellow, E. J., Kim, T. W., Gordon, A. J., Pollio, D. E., Gruzca, R. A., Austin, E. L., ... Kertesz, S. G. (2016). Substance use among persons with homeless experience in primary care. *Substance Abuse*, 37(4), 534–541.
- Stroumsa, D. (2014). The state of transgender health care: Policy, law, and medical frameworks. *American Journal of Public Health*, 104(3), e31–e38.
- Stuard, W. L., Gallerson, B. K., & Robertson, D. M. (2017). Alterations in corneal nerves following crack cocaine use mimic diabetes-induced nerve damage. *Endocrinology, Diabetes, and Metabolism Case Reports*, 2017(1), 16-0131.
- Substance Abuse and Mental Health Services Administration. (n.d.). *Risk and protective factors*. Substance Abuse and Mental Health Services Administration.

- Substance Abuse and Mental Health Services Administration. (2009). *American Indian and Alaska Native culture card: A guide to build cultural awareness*. HHS Publication No. (SMA) 08-4354. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2010). *Recovery-oriented systems of care (ROSC) resource guide* [Working draft]. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2011). *Screening, brief intervention and referral to treatment (SBIRT) in behavioral healthcare*. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2012). *Using Matrix with women clients: A supplement to the Matrix intensive outpatient treatment for people with stimulant use disorders*. HHS Publication No. (SMA) 12-4698. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2013). *Behavioral health services for people who are homeless*. Treatment Improvement Protocol (TIP) Series 55. HHS Publication No. (SMA) 13-4734. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2014). *Improving cultural competence*. Treatment Improvement Protocol (TIP) Series 59. HHS Publication No. (SMA) 14-4849. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2015). Hepatitis C screening in the behavioral healthcare setting. *Advisory*, Vol. 14, Issue 1. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2016). Rural behavioral health: Telehealth challenges and opportunities. *In Brief*, Vol. 9, Issue 2. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2018a). *Behavioral health services for American Indians and Alaska Natives*. Treatment Improvement Protocol (TIP) Series 61. HHS Publication No. (SMA) 18-5070EXSUMM. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2018b). *SAMHSA opioid overdose prevention toolkit*. HHS Publication No. (SMA) 18-4742. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2018c). *Tips for teens: The truth about methamphetamine*. PEP NO. 18-03. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2019). *Enhancing motivation for change in substance use disorder treatment*. Treatment Improvement Protocol (TIP) Series 35. SAMHSA Publication No. PEP19-02-01-003. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2020a). *2018 National Survey on Drug Use and Health: Lesbian, gay, and bisexual (LGB) adults* [Handout showing PowerPoint slides]. Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/sites/default/files/reports/rpt23252/7_LGB_2020_01_14_508.pdf
- Substance Abuse and Mental Health Services Administration. (2020b). *2019 National Survey on Drug Use and Health: African Americans* [Handout showing PowerPoint slides]. Substance Abuse and Mental Health Services Administration. <https://www.samhsa.gov/data/sites/default/files/reports/rpt31099/2019NSDUH-AA/AfricanAmerican%202019%20NSDUH.pdf>
- Substance Abuse and Mental Health Services Administration. (2020c). *2019 National Survey on Drug Use and Health: American Indians and Alaska Natives (AI/ ANs)* [Handout showing PowerPoint slides]. Substance Abuse and Mental Health Services Administration. <https://www.samhsa.gov/data/sites/default/files/reports/rpt31098/2019NSDUH-AIAN/AIAN%202019%20NSDUH.pdf>
- Substance Abuse and Mental Health Services Administration. (2020d). *2019 National Survey on Drug Use and Health: Asian/Native Hawaiians and Other Pacific Islanders (NHOPI)* [Handout showing PowerPoint slides]. Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/sites/default/files/reports/rpt31100/2019NSDUH-NHOPI/Asian_NHOPI.pdf
- Substance Abuse and Mental Health Services Administration. (2020e). *2019 National Survey on Drug Use and Health: Hispanics* [Handout showing PowerPoint slides]. Substance Abuse and Mental Health Services Administration. <https://www.samhsa.gov/data/sites/default/files/reports/rpt31101/2019NSDUH-Hispanic/Hispanic%202019%20NSDUH.pdf>
- Substance Abuse and Mental Health Services Administration. (2020f). *2019 National Survey on Drug Use and Health: Women* [Handout showing PowerPoint slides]. Substance Abuse and Mental Health Services Administration. <https://www.samhsa.gov/data/sites/default/files/reports/rpt31102/2019NSDUH-Women/Women%202019%20NSDUH.pdf>



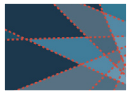
- Substance Abuse and Mental Health Services Administration. (2020g). *Key substance use and mental health indicators in the United States: Results from the 2019 National Survey on Drug Use and Health*. NSDUH Series H-55. HHS Publication No. PEP20-07-01-001. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2020h). *Medications for opioid use disorder*. Treatment Improvement Protocol (TIP) Series 63. Publication No. PEP20-02-01-006. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2020i). *The opioid crisis and the Black/African American population: An urgent issue*. Publication No. PEP20-05-02-001. Office of Behavioral Health Equity. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2020j). *Prevention and treatment of HIV among people living with substance use and/or mental disorders*. Publication No. PEP20-06-03-001. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2020k). *Substance use disorder treatment and family therapy*. Treatment Improvement Protocol (TIP) Series 39. SAMHSA Publication No. PEP20-02-02-012. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2020l). *Substance use disorder treatment for people with co-occurring disorders*. Treatment Improvement Protocol (TIP) Series 42. SAMHSA Publication No. PEP20-02-01-004. Substance Abuse and Mental Health Services Administration.
- Substance Abuse and Mental Health Services Administration. (2020m). *Treatment of stimulant use disorders*. SAMHSA Publication No. PEP20-06-01-001. Substance Abuse and Mental Health Services Administration, National Mental Health and Substance Use Policy Laboratory.
- Substance Abuse and Mental Health Services Administration. (2020n, August 19). Co-occurring disorders and other health conditions. <https://www.samhsa.gov/medication-assisted-treatment/medications-counseling-related-conditions/co-occurring-disorders>
- Substance Abuse and Mental Health Services Administration. (2020o, September 15). Naltrexone. <https://www.samhsa.gov/medication-assisted-treatment/medications-counseling-related-conditions/naltrexone>
- Substance Abuse and Mental Health Services Administration. (2021a). Integrating vocational services into substance use disorder treatment. *Advisory*.
- Substance Abuse and Mental Health Services Administration. (2021b). Using technology-based therapeutic tools in behavioral health services. *Advisory*.
- Substance Abuse and Mental Health Services Administration. (2021c, February 5). ASAM criteria. <https://www.samhsa.gov/resource/ebp/asam-criteria>
- Swann, A. C. (2010). The strong relationship between bipolar and substance-use disorder. *Annals of the New York Academy of Sciences*, 1187(2010), 276–293.
- Swanson, J., Baler, R. D., & Volkow, N. D. (2011). Understanding the effects of stimulant medications on cognition in individuals with attention-deficit hyperactivity disorder: A decade of progress. *Neuropsychopharmacology*, 36(1), 207–226.
- Szerman, N., Ferre, F., Basurte-Villamor, I., Vega, P., Mesias, B., Marín-Navarrete, R., & Arango, C. (2020). Gambling dual disorder: A dual disorder and clinical neuroscience perspective. *Frontiers in Psychiatry*, 11, 589155.
- Szydlowski, S. J., & Amato, P. P. (2017). Nutrition in addiction treatment. *Journal of Traditional Medicine and Clinical Naturopathy*, 6, 218.
- Tait, R. J., McKetin, R., Kay-Lambkin, F., Carron-Arthur, B., Bennett, A., Bennett, K., ... Griffiths, K. M. (2015). Six-month outcomes of a web-based intervention for users of amphetamine-type stimulants: Randomized controlled trial. *Journal of Medical Internet Research*, 17(4), e105.
- Tavitian-Exley, I., Vickerman, P., Bastos, F. I., & Boily, M.-C. (2015). Influence of different drugs on HIV risk in people who inject: Systematic review and meta-analysis. *Addiction*, 110(4), 572–584.
- Taylor, S. B., Lewis, C. R., & Olive, M. F. (2013). The neurocircuitry of illicit psychostimulant addiction: Acute and chronic effects in humans. *Substance Abuse and Rehabilitation*, 4, 29–43.
- Tech-enabled CM for AUD at scale in Medicaid. (2020). (Identification No. NCT04581499). <https://clinicaltrials.gov/ct2/show/NCT04581499>
- Telzer, E. H. (2016). Dopaminergic reward sensitivity can promote adolescent health: A new perspective on the mechanism of ventral striatum activation. *Developmental Cognitive Neuroscience*, 17, 57–67.
- Teran, R. A., Carrico, A. W., Horvath, K. J., Downing, Jr., M. J., Chiasson, M. A., Walters, S. M., & Hirshfield, S. (2020). Stimulant use and study protocol completion: Assessing the ability of men who have sex with men to collect dried blood spots for laboratory measurement of HIV viral load. *Archives of Sexual Behavior*, 49(1), 195–209.
- Terlizzi, E. P., & Villarreal, M. A. (2020). *Symptoms of generalized anxiety disorder among adults: United States, 2019* (NCHS Data Brief, No. 378). National Center for Health Statistics.

- Tetrault, J. M., McCance-Katz, E. F., Moody, D. E., Fiellin, D. A., Lruie, B. S., Dlnh, A. T., & Fiellin, L. E. (2015). The impact of recent cocaine use on plasma levels of methadone and buprenorphine in patients with and without HIV-infection. *Journal of Substance Abuse Treatment*, 51, 70–74.
- Thomas, D. M., Pérez, M. A., Francescutti-Verbeem, D. M., Shah, M. M., & Kuhn, D. M. (2010). The role of endogenous serotonin in methamphetamine-induced neurotoxicity to dopamine nerve endings of the striatum. *Journal of Neurochemistry*, 115(3), 595–605.
- Thompson, R. G., Jr., & Auslander, W. F. (2011). Substance use and mental health problems as predictors of HIV sexual risk behaviors among adolescents in foster care. *Health and Social Work*, 36(1), 33–43.
- Timko, C., Booth, B. M., Han, X., Schultz, N. R., Blonigen, D. M., Wong, J. J., & Cucciare, M. A. (2017). Criminogenic needs, substance use, and offending among rural stimulant users. *Rural Mental Health*, 41(2), 110–122.
- Timko, C., Han, X., Woodhead, E., Shelley, A., & Cucciare, M. A. (2018). Polysubstance use by stimulant users: Health outcomes over three years. *Journal of Studies on Alcohol and Drugs*, 79(5), 799–807.
- Timko, C., Schultz, N. R., Britt, J., & Cucciare, M. A. (2016). Transitioning from detoxification to substance use disorder treatment: Facilitators and barriers. *Journal of Substance Abuse Treatment*, 70, 64–72.
- To protect and serve: Joint law enforcement efforts in building safe tribal communities and stopping dangerous drugs from entering Indian Country, U.S. Senate Committee on Indian Affairs. 116th Cong. (2019) (testimony of Charles Addington).
- Tolliver, B. K., McRae-Clark, A. L., Saladin, M., Price, K. L., Simpson, A. N., DeSantis, S. M., ... Brady, K. T. (2010). Determinants of cue-elicited craving and physiologic reactivity in methamphetamine-dependent subjects in the laboratory. *American Journal of Drug and Alcohol Abuse*, 36(2), 106–113.
- Tong, H. Y., Díaz, C., Collantes, E., Medrano, N., Borobia, A. M., Jara, P., & Ramírez, E. (2015). Liver transplant in a patient under methylphenidate therapy: A case report and review of the literature. *Case Reports in Pediatrics*, 2015, 437298.
- Tonigan, J. S., Venner, K., & Hirschak, K. A. (2020). Urban American Indian adult participation and outcomes in culturally adapted and mainstream *Alcoholics Anonymous meetings*. *Alcohol Treatment Quarterly*, 38(1), 50–67.
- Torchalla, I., Strehlau, V., Li, K., & Krausz, M. (2011). Substance use and predictors of substance dependence in homeless women. *Drug and Alcohol Dependence*, 118(2–3), 173–179.
- Torregrossa, M. M., & Taylor, J. R. (2013). Learning to forget: Manipulating extinction and reconsolidation processes to treat addiction. *Psychopharmacology*, 226(4), 659–672.
- Torres, T. S., Bastos, L. S., Kamel, L., Bezerra, D. R. B., Fernandes, N. M., Moreira, R. I., ... De Boni, R. B. (2020). Do men who have sex with men who report alcohol and illicit drug use before/during sex (chemsex) present moderate/high risk for substance use disorders? *Drug and Alcohol Dependence*, 209, 107908.
- Torres-Acosta, N., O'Keefe, J. H., O'Keefe, C. L., & Lavie, C. J. (2020). Cardiovascular effects of ADHD therapies: JACC Review Topic of the Week. *Journal of the American College of Cardiology*, 76(7), 858–866.
- Tracy, D., Hahn, J. A., Fuller Lewis, C., Evans, J., Briceño, A., Morris, M. D., ... Page, K. (2014). Higher risk of incident hepatitis C virus among young women who inject drugs compared with young men in association with sexual relationships: A prospective analysis from the UFO Study cohort. *BMJ Open*, 4(5), e004988.
- Trauma Informed Oregon. (2019). *Trauma informed urine drug screenings*.
- Tressler, S. R., Kushner, T., & Bhandari, R. (2020). Factors associated with hepatitis B exposure among people who report using methamphetamine: National Health and Nutrition Examination Survey 2009–2016. *Journal of Infectious Diseases*, 221(2), 243–250.
- Trivedi, M. H., Greer, T. L., Rethorst, C. D., Carmody, T., Grannemann, B. D., Walker, R., ... Nunes, E. V. (2017). Randomized controlled trial comparing exercise to health education for stimulant use disorder: Results from the CTN-0037 STimulant Reduction Intervention Using Dosed Exercise (STRIDE) study. *Journal of Clinical Psychiatry*, 78(8), 1075–1082.
- Tsai, H., Lee, J., Hedlin, H., Zamanian, R. T., & de Jesus Perez, V. A. (2019). Methamphetamine use association with pulmonary diseases: A retrospective investigation of hospital discharges in California from 2005 to 2011. *ERJ Open Research*, 5(4), 00017-2019.
- Tsai, J., & Gu, X. (2019). Utilization of addiction treatment among U.S. adults with history of incarceration and substance use disorders. *Addiction Science and Clinical Practice*, 14, 9.
- Tsui, J. I., Mayfield, J., Speaker, E. C., Yakup, S., Ries, R., Funai, H., ... Merrill, J. O. (2020). Association between methamphetamine use and retention among patients with opioid use disorders treated with buprenorphine. *Journal of Substance Abuse Treatment*, 109, 80–85.
- Turowski, P., & Kenny, B.-A. (2015). The blood-brain barrier and methamphetamine: Open sesame? *Frontiers in Neuroscience*, 9, 156.



- United Nations Office on Drugs and Crime. (2018). *World drug report 2018: Drugs and age* (Booklet 4).
- United Nations Office on Drugs and Crime. (2019a). *HIV prevention, treatment, care and support for people who use stimulant drugs* [Technical guide].
- United Nations Office on Drugs and Crime. (2019b). *Treatment of stimulant use disorders: Current practices and promising perspectives* [Discussion paper].
- United Nations Population Fund, Global Forum on MSM & HIV, United Nations Development Programme, World Health Organization, U.S. Agency for International Development, World Bank. (2015). *Implementing comprehensive HIV and STI programmes with men who have sex with men: Practical guidance for collaborative interventions*. United Nations Population Fund.
- University of Michigan. (2020). *Monitoring the Future Survey: 2020 data from in-school surveys of 8th-, 10th-, and 12th-grade students* [Data set]. <http://www.monitoringthefuture.org/data/20data.html#2020data-drugs>
- Upshur, C. C., Jenkins, D., Weinreb, L., Gelberg, L., & Orvek, E. A. (2018). Homeless women's service use, barriers, and motivation for participating in substance use treatment. *American Journal of Drug and Alcohol Abuse*, 44(2), 252–262.
- U.S. Census Bureau. (n.d.). United States. Retrieved June 22, 2021, from <https://data.census.gov/cedsci/profile?q=United%20States&g=0100000US>
- U.S. Preventive Services Task Force. (2020a). *Final recommendation statement: Hepatitis C virus infection in adolescents and adults: Screening*. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hepatitis-c-screening>
- U.S. Preventive Services Task Force. (2020b). *Final recommendation statement: Screening for hepatitis B virus infection in adolescents and adults*. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/hepatitis-b-virus-infection-screening>
- Vanderplasschen, W., Rapp, R. C., De Maeyer, J., & Van Den Noortgate, W. (2019). A meta-analysis of the efficacy of case management for substance use disorders: A recovery perspective. *Frontiers in Psychiatry*, 10, 186.
- Vasan, S., & Olango, G. J. (2020). Amphetamine toxicity. In *StatPearls*. Retrieved March 19, 2021, from <https://www.ncbi.nlm.nih.gov/books/NBK470276/>
- Vayalapalli, S., Fareed, A., Casarella, J., & Drexler, K. (2011). Housing as a motivation for seeking substance abuse treatment. *American Journal on Addictions*, 20(2), 182–183.
- Verma, V. (2015). Classic studies on the interaction of cocaine and the dopamine transporter. *Clinical Psychopharmacology and Neuroscience*, 13(3), 227–238.
- Visconti, A. J., Sell, J., & Greenblatt, A. D. (2019). Primary care for persons who inject drugs. *American Family Physician*, 99(2), 109–116.
- Visser, S. N., Danielson, M. L., Bitsko, R. H., Holbrook, J. R., Kogan, M. D., Ghandour, R. M., ... Blumberg, S. J. (2014). Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United States, 2003–2011. *Journal of the American Academy of Child and Adolescent Psychiatry*, 53(1), 34–46.e2.
- Viswanath, H., Wilkerson, J. M., Breckenridge, E., & Selwyn, B. J. (2017). Life chaos and perceived social support among methamphetamine-using men who have sex with men engaging in transactional sexual encounters. *Substance Use and Misuse*, 52(1), 100–107.
- Volkow, N. D., Baler, R. D., Compton, W. M., & Weiss, S. R. (2014). Adverse health effects of marijuana use. *New England Journal of Medicine*, 370(23), 2219–2227.
- Volkow, N. D., Michaelides, M., & Baler, R. (2019). The neuroscience of drug reward and addiction. *Physiological Reviews*, 99(4), 2115–2140.
- Volkow, N. D., Wang, G. J., Fowler, J. S., Telang, F., Jayne, M., & Wong, C. (2007). Stimulant-induced enhanced sexual desire as a potential contributing factor in HIV transmission. *American Journal of Psychiatry*, 164(1), 157–160.
- Volkow, N. D., Wise, R. A., & Baler, R. (2017). The dopamine motive system: Implications for drug and food addiction. *Nature Reviews Neuroscience*, 18(12), 741–752.
- Vonmoos, M., Hulka, L. M., Preller, K. H., Minder, F., Baumgartner, M. R., & Quednow, B. B. (2014). Cognitive impairment in cocaine users is drug-induced but partially reversible: Evidence from a longitudinal study. *Neuropsychopharmacology*, 39(9), 2200–2210.
- Vosburg, S. K., Haney, M., Rubin, E., & Foltin, R. W. (2010). Using a novel alternative to drug choice in a human laboratory model of a cocaine binge: A game of chance. *Drug and Alcohol Dependence*, 110(1–2), 144–150.
- Vu, N. T., Maher, L., & Zablotska, I. (2015). Amphetamine-type stimulants and HIV infection among men who have sex with men: Implications on HIV research and prevention from a systematic review and meta-analysis. *Journal of the International AIDS Society*, 18(1), 19273.
- Vujanovic, A. A., Bonn-Miller, M. O., & Petry, N. M. (2016). Co-occurring posttraumatic stress and substance use: Emerging research on correlates, mechanisms, and treatments—Introduction to the special issue. *Psychology of Addictive Behaviors*, 30(7), 713–719.

- Walley, A. (2013). *Stimulants: Cocaine and methamphetamine* [Handout showing PowerPoint slides]. Presentation at the Resident Immersion Training (CRIT) Program in Addiction Medicine at Boston University School of Medicine. <https://www.bumc.bu.edu/care/files/2013/06/4.-A.-WALLEY-STIMULANTS-CRIT-FIT-20132.pdf>
- Walls, N. E., & Bell, S. (2011). Correlates of engaging in survival sex among homeless youth and young adults. *Journal of Sex Research, 48*(5), 423–436.
- Walsh-Buhi, M. L. (2017). "Please don't just hang a feather on a program or put a medicine wheel on your logo and think 'Oh well, this will work'": Theoretical perspectives of American Indian and Alaska Native substance abuse prevention programs. *Family Community Health, 40*(1), 81–87.
- Wang, L., Min, J. E., Krebs, E., Evans, E., Huang, D., Liu, L., ... Nosyk, B. (2017). Polydrug use and its association with drug treatment outcomes among primary heroin, methamphetamine, and cocaine users. *International Journal on Drug Policy, 49*, 32–40.
- Warden, D. W., Sanchez, K., Greer, T., Carmody, T. Walker, R., dela Cruz, A., ... Trivedi, M. H. (2016). Demographic and clinical characteristics of current comorbid psychiatric disorders in a randomized clinical trial for adults with stimulant use disorders. *Psychiatry Research, 246*, 136–141.
- Wassum, K. M., & Izquierdo, A. (2015). The basolateral amygdala in reward learning and addiction. *Neuroscience and Biobehavioral Reviews, 57*, 271–283.
- Waye, K. M., Goyer, J., Dettor, D., Mahoney, L., Samuels, E. A., Yedinak, J. L., & Marshall, B. (2019). Implementing peer recovery services for overdose prevention in Rhode Island: An examination of two outreach-based approaches. *Addictive Behaviors, 89*, 85–91.
- Wearne, T. A., & Cornish, J. L. (2018). A comparison of methamphetamine-induced psychosis and schizophrenia: A review of positive, negative, and cognitive symptomatology. *Frontiers in Psychiatry, 9*, 491.
- Weinstein, Z. M., Kim, H. W., Cheng, D. M., Quinn, E., Hui, D., Labelle, C. T., & Samet, J. H. (2017). Long-term retention in office based opioid treatment with buprenorphine. *Journal of Substance Abuse Treatment, 74*, 65–70.
- Weintraub, E., Greenblatt, A. D., Chang, J., Himelhoch, S., & Welsh, C. (2018). Expanding access to buprenorphine treatment in rural areas with the use of telemedicine. *American Journal on Addictions, 27*(8), 612–617.
- Werb, D., Buxton, J., Shoveller, J., Richardson, C., Rowell, G., & Wood, E. (2013). Interventions to prevent the initiation of injection drug use: A systematic review. *Drug and Alcohol Dependence, 133*(2), 669–676.
- Werner, F. M., & Covenas, R. (2017). Long-term administration of antipsychotic drugs in schizophrenia and influence of substance and drug abuse on the disease outcome. *Current Drug Abuse Reviews, 10*(1), 19–24.
- Westover, A. N., & Halm, E. A. (2012). Do prescription stimulants increase the risk of adverse cardiovascular events?: A systematic review. *BMC Cardiovascular Disorders, 12*(1), 1–10.
- Weyandt, L. L., Marraccini, M. E., Gudmundsdottir, B. G., Zavras, B. M., Turcotte, K. D., Munro, B. A., & Amoroso, A. J. (2013). Misuse of prescription stimulants among college students: A review of the literature and implications for morphological and cognitive effects on brain functioning. *Experimental and Clinical Psychopharmacology, 21*(5), 385–407.
- Weyandt, L. L., Oster, D. R., Marraccini, M. E., Gudmundsdottir, B. G., Munro, B. A., Rathkey, E. S., & McCallum, A. (2016). Prescription stimulant medication misuse: Where are we and where do we go from here? *Experimental and Clinical Psychopharmacology, 24*(5), 400–414.
- Weyandt, L. L., White, T. L., Gudmundsdottir, B. G., Nitenson, A. Z., Rathkey, E. S., De Leon, K. A., & Bjorn, S. A. (2018). Neurocognitive, autonomic, and mood effects of Adderall: A pilot study of healthy college students. *Pharmacy, 6*(3), 58.
- White, W. (2004). History of drug problems and drug policies in America. In R. Coombs (Ed.), *Addiction counseling review: Preparing for comprehensive certification exams* (pp. 81–104). Lahaska Press.
- Whitesell, N. R., Beals, J., Big Crow, C. B., Mitchell, C. M., & Novins, D. K. (2012). Epidemiology and etiology of substance use among American Indians and Alaska Natives: Risk, protection, and implications for prevention. *American Journal of Drug and Alcohol Abuse, 38*(5), 376–382.
- Wiener, S. E., Sutijono, D., Moon, C. H., Subramanian, R. A., Calaycay, J., Rushbrook, J. I., & Zehtabchi, S. (2010). Patients with detectable cocaethylene are more likely to require intensive care unit admission after trauma. *American Journal of Emergency Medicine, 28*(9), 1051–1055.
- Wiers, C. E., Cabrera, E., Skarda, E., Volkow, N. D., & Wang, G. J. (2016). PET imaging for addiction medicine: From neural mechanisms to clinical considerations. *Progress in Brain Research, 224*, 175–201.
- Wiggs, K. K., Chang, Z., Quinn, P. D., Hur, K., Gibbons, R., Dunn, D., ... D'Onofrio, B. M. (2018). Attention-deficit/hyperactivity disorder medication and seizures. *Neurology, 90*(13), e1104–e1110.



- Wilens, T. E., Carrellas, N. W., Martelon, M., Yule, A. M., Fried, R., Anselmo, R., & McCabe, S. E. (2017). Neuropsychological functioning in college students who misuse prescription stimulants. *American Journal on Addictions*, 26(4), 379–387.
- Wilens, T. E., Martelon, M., Joshi, G., Bateman, C., Fried, R., Petty, C., & Biederman, J. (2011). Does ADHD predict substance-use disorders? A 10-year follow-up study of young adults with ADHD. *Journal of the American Academy of Child and Adolescent Psychiatry*, 50(6), 543–553.
- Wilens, T., Zulauf, C., Martelon, M., Morrison, N. R., Simon, A., Carrellas, N. W., ... Anselmo, R. (2016). Nonmedical stimulant use in college students: Association with attention-deficit/hyperactivity disorder and other disorders. *Journal of Clinical Psychiatry*, 77(7), 940–947.
- Wilkerson, A. K., Sahlem, G. L., Bentzley, B. S., Lord, J., Smith, J. P., Simmons, R. O., ... Book, S. W. (2019). Insomnia severity during early abstinence is related to substance use treatment completion in adults enrolled in an intensive outpatient program. *Journal of Substance Abuse Treatment*, 104, 97–103.
- Wilkerson, J. M., Noor, S. W., Rhoton, J. M., Li, D., & Rosser, B. R. S. (2018). Differentially classified methamphetamine-using men who have sex with men: A latent class analysis. *Drug and Alcohol Dependence*, 192, 129–136.
- Wimberly, A. S., Hyatt, J. M., & McKay, J. R. (2018). Effect of continuing care for people with cocaine dependence on criminal justice sentences. *Behavioral Sciences and the Law*, 36(1), 116–129.
- Winkelman, T. N. A., Admon, L. K., Jennings, L., Shippee, N. D., Richardson, C. R., & Bart, G. (2018). Evaluation of amphetamine-related hospitalizations and associated clinical outcomes and costs in the United States. *JAMA Network Open*, 1(6), e183758.
- Winn, L. A. P., Paquette, K. L., Donegan, L. R. W., Wilkey, C. M., & Ferreira, K. N. (2019). Enhancing adolescent SBIRT with a peer-delivered intervention: An implementation study. *Journal of Substance Abuse Treatment*, 103, 14–22.
- Wise, R. A. (2008). Dopamine and reward: The anhedonia hypothesis 30 years on. *Neurotoxicity Research*, 14(2–3), 169–183.
- Wise, R. A., & Koob, G. F. (2014). The development and maintenance of drug addiction. *Neuropsychopharmacology*, 39(2), 254–262.
- Wiss, D. A. (2019). The role of nutrition in addiction recovery: What we know and what we don't. In I. Danovitch & L. J. Mooney (Eds.), *The assessment and treatment of addiction* (pp. 21–42). Elsevier.
- Wood, S., Sage, J. R., Shuman, T., & Anagnostaras, S. G. (2014). Psychostimulants and cognition: A continuum of behavioral and cognitive activation. *Pharmacological Reviews*, 66(1), 193–221.
- Woolum, J. A., Travis, M., Running Cranem, C., Bailey, A. M., Baum, R. A., & Akpunonu, P. (2019). Use of lidocaine for treatment of pulseless ventricular tachycardia after massive cocaine overdose. *Toxicology Communications*, 3(1), 19–22.
- Workowski, K. A., & Bolan, G. A. (2015). Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recommendations and Reports*, 64(RR-3), 1–137.
- World Health Organization & United Nations Office on Drugs and Crime. (2020). *International standards for the treatment of drug use disorders: Revised edition incorporating results of field testing*. <https://www.who.int/publications/i/item/international-standards-for-the-treatment-of-drug-use-disorders>
- Worley, J. (2014). Identification and management of prescription drug abuse in pregnancy. *Journal of Perinatal and Neonatal Nursing*, 28(3), 196–203.
- Wright, T. E., Schuetter, R., Tellei, J., & Sauvage, L. (2015). Methamphetamines and pregnancy outcomes. *Journal of Addiction Medicine*, 9(2), 111–117.
- Wu, L. T., Pan, J. J., Blazer, D. G., Tai, B., Stitzer, M. L., & Woody, G. E. (2010). Using a latent variable approach to inform gender and racial/ethnic differences in cocaine dependence: A National Drug Abuse Treatment Clinical Trials Network Study. *Journal of Substance Abuse Treatment*, 38(Suppl. 1), S70–S79.
- Wunderli, M. D., Vonmoos, M., Niedecker, S. M., Hulka, L. M., Preller, K. H., Baumgartner, M. R., ... Quednow, B. B. (2016). Cognitive and emotional impairments in adults with attention-deficit/hyperactivity disorder and cocaine use. *Drug and Alcohol Dependence*, 163, 92–99.
- Yang, X., Wang, Y., Li, Q., Zhong, Y., Chen, L., Du, Y., ... Yan, J. (2018). The main molecular mechanisms underlying methamphetamine-induced neurotoxicity and implications for pharmacological treatment. *Frontiers in Molecular Neuroscience*, 11, 186.
- Yanofski, J. (2011). The dopamine dilemma—Part II: Could stimulants cause tolerance, dependence, and paradoxical decompensation? *Innovations in Clinical Neuroscience*, 8(1), 47–53.
- Yasaei, R., & Saadabadi, A. (2021). Methamphetamine. In *StatPearls*. Retrieved June 1, 2021, from <https://www.ncbi.nlm.nih.gov/books/NBK535356/>
- Yazdani, M., Armoon, B., Noroozi, A., Mohammadi, R., Bayat, A. H., Ahounbar, E., ... Hemmat, M. (2020). Dental caries and periodontal disease among people who use drugs: A systematic review and meta-analysis. *BMC Oral Health*, 20(1), 44.
- Ye, L., Peng, J. S., Wang, X., Wang, Y. J., Luo, G. X., & Ho, W. Z. (2008). Methamphetamine enhances hepatitis C virus replication in human hepatocytes. *Journal of Viral Hepatitis*, 15(4), 261–270.

- Yee, T., Perantie, D. C., Dhanani, N., & Brown, E. S. (2004). Drug dreams in outpatients with bipolar disorder and cocaine dependence. *Journal of Nervous and Mental Disease*, 192(3), 238–242.
- Yeung, J. T., Williams, J., & Bowling, W. M. (2013). Effect of cocaine use on outcomes in traumatic brain injury. *Journal of Emergencies, Trauma, and Shock*, 6(3), 189–194.
- Yoshioka-Maxwell, A., Rice, E., Rhoades, H., & Winetrobe, H. (2015). Methamphetamine use among homeless former foster youth: The mediating role of social networks. *Journal of Alcoholism and Drug Dependence*, 3(2), 197.
- Young, D., & Scoville, W. B. (1938). Paranoid psychosis in narcolepsy and the possible danger of enzedrine treatment. *Medical Clinics of North America*, 22, 637–646.
- Young, L. B., Grant, K. M., & Tyler, K. A. (2015). Community-level barriers to recovery for substance-dependent rural residents. *Journal of Social Work Practice in the Addictions*, 15(3), 307–326.
- Younger, D. S. (2019). Central nervous system vasculitis due to substance abuse. *Neurologic Clinics*, 37(2), 425–440.
- Yu, G., Wall, M. M., Chiasson, M. A., & Hirshfield, S. (2015). Complex drug use patterns and associated HIV transmission risk behaviors in an Internet sample of U.S. men who have sex with men. *Archives of Sexual Behavior*, 44(2), 421–428.
- Zapolski, T. C. B., Baldwin, P. D., & Lejuez, C. W. (2016). Examining risk for frequent cocaine use: Focus on an African American treatment population. *Substance Use and Misuse*, 51(7), 882–891.
- Zhang, S. X., Shoptaw, S., Reback, C. J., Yadav, K., & Nyamathi, A. M. (2018). Cost-effective way to reduce stimulant-abuse among gay/bisexual men and transgender women: A randomized clinical trial with a cost comparison. *Public Health*, 154, 151–160.
- Zhou, C., Crawford, A., Serhal, E., Kurdyak, P., & Sockalingam, S. (2016). The impact of Project ECHO on participant and patient outcomes: A systematic review. *Academic Medicine*, 91(10), 1439–1461.
- Zhu, Y., Evans, E. A., Mooney, L. J., Saxon, A. J., Kelleghan, A., Yoo, C., & Hser, Y.-I. (2018). Correlates of long-term opioid abstinence after randomization to methadone versus buprenorphine/naloxone in a multi-site trial. *Journal of Neuroimmune Pharmacology*, 13, 488–497.
- Zimmerman, J. L. (2012). Cocaine intoxication. *Critical Care Clinics*, 28(4), 517–526.
- Zorick, T., Nestor, L., Miotto, K., Sugar, C., Hellemann, G., Scanlon, G., ... London, E. D. (2010). Withdrawal symptoms in abstinent methamphetamine-dependent subjects. *Addiction*, 105(10), 1809–1818.
- Zwick, J., Appleseth, H., & Arndt, S. (2020). Stigma: How it affects the substance use disorder patient. *Substance Abuse Treatment, Prevention, and Policy*, 15(1), 50.

SAMHSA Publication No. PEP21-02-01-004
First released 1999. Revised 2021.

Substance Abuse and Mental Health Services Administration
SAMHSA's mission is to reduce the impact of substance abuse
and mental illness on America's communities.

1-877-SAMHSA-7 (1-877-726-4727) | 1-800-486-4889 (TDD)
www.samhsa.gov

SAMHSA
Substance Abuse and Mental Health
Services Administration